YEARLY SUBSCRIPTION, $6.00

SEP 27 192?

SINGLE NUMBERS $1.00

THE AMERICAN JOURNAL OF ROENTGENOLOGY

[FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY]

OFFICIAL ORGAN OF
THE AMERICAN ROENTGEN RAY SOCIETY
AND THE AMERICAN RADIUM SOCIETY

Editor: H. M. IMBODEN, M.D.

Associate Editors:

JAMES T. CASE, M.D. H. K. PANCOAST, M.D. J. S. SHEARER, PH.D.

EDITORIAL BOARD

FREDERICK H. BAETJER, M.D.
A. BECLERE, M.D.
DAVID R. BOWEN, M.D.
PERCY BROWN, M.D.
R. D. CARMAN, M.D.
L. G. COLE, M.D.
A. W. CRANE, M.D.
A. W. GEORGE, M.D.
PRESTON M. HICKEY, M.D.
ROBERT KNOX, M.D.
R. LEDOUX-LEBARD, M.D.
G. E. PFAHLER, M.D.
A. H. PIRIE, M.D.
E. H. SKINNER, M.D.

VOLUME IX NUMBER 9

September, 1922

PUBLISHED MONTHLY BY PAUL B. HOEBER
NEW YORK CITY

TWENTY-THIRD ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY WILL BE HELD AT LOS ANGELES, CAL., SEPTEMBER 12, 13, 14, 15, 16, 1922

Entered as second-class matter, March 3, 1916, at the Post Office, New York, N. Y., under the Act of March 3, 1879.

TROLLEYLESS Clinix X-RAY PLANT

ANNOUNCEMENT

THE CLINIX AFTER TWO YEARS in the X-Ray field is still the only TROLLEYLESS and the finest piece of X-Ray Apparatus ever thought of.

THE CLINIX PRINCIPLE is now universally accepted.

IT IS PROTECTED by the following:

U. S. Patents December 19, 1911. April 22, 1913. February 29, 1916. August 7, 1917. Also patented in foreign countries. Other patents pending. Infringers will be prosecuted.

Beware of infringement as no other manufacturer is licensed to use CAMPBELL patents and no reliable manufacturer would dare infringe.

PRODUCTION OF THE CLINIX is on a larger scale than ever before attempted in the manufacture of similar apparatus.

MANY REFINEMENTS have been added since the CLINIX first made its appearance.

THE CLINIX SAVES { Office Rent / Original Investment / Lives

BECAUSE IT IS { Compact / Complete / Trolleyless

Investigate Campbell ELECTRIC CO. LYNN, MASS *Send for Catalog*

William H. Stewart

PRESIDENT OF THE AMERICAN ROENTGEN RAY SOCIETY
1922-1923

THE AMERICAN JOURNAL OF ROENTGENOLOGY

VOL. IX [NEW SERIES] SEPTEMBER, 1922 No. 9

THE ROENTGENOLOGICAL ASPECTS OF ACHYLIA GASTRICA*

BY A. W. CRANE, M.D.

KALAMAZOO, MICHIGAN

EVERY form of alimentary tract pathology must ultimately be considered in its relations to roentgenological signs. Gastric and duodenal ulcers which are usually associated with an increased secretion of hydrochloric acid are the most studied and the best understood roentgenologically of all gastrointestinal diseases. We have now to consider the roentgen-ray interpretation of an opposite secretory condition, namely, a total absence of free hydrochloric acid which is associated with a wide range of diseases and with signs and symptoms which may lead easily to diagnostic confusion. We shall in achylia encounter six-hour residues without gastric ulcer; or we may find vigorous, bisecting peristalsis and rapid expulsion of stomach contents without ulcer of the duodenum. The patient may complain of recurring epigastric hunger pain as in ulcer, or right hypogastric pain as in cholecystitis, or a deep vague abdominal pain as in cancer, and yet no roentgenological sign of any gastrointestinal pathology may be discoverable. Especially in achylia the complaint may be a persistent pain below the left costal margin, which is the despair of the diagnostician. A study of the laboratory analyses may thus furnish the roentgenologist with the deciding factor in the interpretation of the *x*-ray findings and prevent unduly radical conclusions from indecisive signs.

The term achylia gastrica, although originally introduced by Einhorn to mean a total absence of the gastric juice, is now commonly used in medical literature to mean a total absence of free hydrochloric acid. Barker ("Monographic Medicine," iii, 516) states that in the early stages of achylia the gastric ferments are still present. He also says that the use of the term achylia to mean the absence of free acid is growing. Many authors shun the word achylia and use achlorhydria to mean the absence of free acid. But the continued use of the term achylia gastrica indicates a real need. This term implies an organic change and constitutes a diagnosis, whereas achlorhydria implies a purely functional alteration of gastric secretion, and is never a diagnosis. Hyperacidity is an example of a functional change which may disappear under treatment with a return to the normal; but achylia gastrica once established is, with surprisingly few exceptions, a permanent condition, with organic changes in the stomach walls. In this respect it is on a par as a diagnostic concept with a valvular disease of the heart in the course of a goiter, a nephritis following a focal infection, or an arteriosclerosis resulting from luetic disease. Achylia gastrica similarly results from, or is associated with pernicious anemia, cancer, dental sepsis, gall-stones, intestinal toxemias and a number of other apparently unrelated diseases. In this paper, therefore, the term achylia gastrica is used

*Read at the Midwinter Meeting of the Central Section of THE AMERICAN ROENTGEN RAY SOCIETY, Chicago, Ill., February 22, 1922.

to mean an established chronic disease of the stomach characterized by the persistent absence of free hydrochloric acid in the stomach contents during the whole of the digestive cycle.

The material which forms the basis of this study consists of approximately 1,000 cases in which, with few exceptions, the stomach contents were obtained in 5 or 6 fractions at fifteen-minute intervals, beginning one-half hour after the Ewald test meal. These cases were examined in collaboration with my partner, Dr. John B. Jackson, and with the help of several very capable assistants. The case records contain the histories, physical examinations, laboratory analyses of the blood, urine, stomach contents and other material when available, in addition to the *x*-ray examinations, excepting in a few cases where these were considered unnecessary.

The importance of achylia to the roentgenologist lies in the following points:

1. Its frequency in gastrointestinal cases.
2. Its association with abdominal pain.
3. Its association with intestinal disturbances.
4. The difference in the interpretation of the same roentgen-ray signs according to whether or not achylia is present.

The frequency of achylia is surprising and increases rapidly with increasing age. Lockwood, in a careful analysis of 500 cases in his personal practice, found that in patients over fifty years of age 60 per cent showed achylia. He quotes Stockton as finding 37 per cent and Seidelin 40 per cent under similar conditions and criticises their figures as too low. For patients between twenty and seventy years of age Lockwood's figures show 17.4 per cent of achylia. In the 1,000 cases which comprise our own series 12.6 per cent of achylia was found for all ages. It is, therefore, an almost daily problem in gastrointestinal diagnosis.

It is, however, less frequent in our series than hyperacidity. Of our 1,000 cases, 158 showed achylia compared with 393 showing hyperacidity. Of these 393 cases, 117 showed duodenal ulcer and 25 gastric ulcer, but of the 158 cases of achylia not a single case of ulcer was diagnosticated or found later by subsequent examination, operation or autopsy. In some of the reported cases of peptic ulcer in achylia the diagnosis of achylia has been based upon a single sample of the stomach contents. This may give false conclusions, as many writers have pointed out. In our series a total absence of hydrochloric acid may be found in several of the first samples, and yet an hyperacidity develop in the final samples obtained by the Rehfuss fractional tube. Granting, however, that peptic ulcer does occur in achylia gastrica we may emphasize the conclusion that the occurrence is exceedingly rare.

The association of pain with achylia arrests attention. In all, 102 out of the 158 cases complained of pain which, in 69 cases, was abdominal. The source of this pain was often difficult to find and sometimes inexplicable. The pains of hyperacidity are, with few exceptions, attributable directly to peptic ulcer or pylorospasm; but the pain associated with achylia in our series was in no case due to either of these causes. Only in 26 cases of gastric cancer and the one of gastric syphilis was the pain due to any demonstrable condition within the stomach. In 17 cases the pain was traced to the gall-bladder, in 9 cases to the appendix and in 8 cases to pericolic adhesions. Mucous colitis was present in two cases. Spondylitis deformans, which is a possible cause of abdominal pain, was demonstrated in 11 cases, 5 of which complained of pain in the abdomen. The explanation of the pain is often questionable even when the examination is sufficiently thorough. The diversity of causes and the number of achylias without pain make it doubtful if the achylia itself is often accountable for it. The useful conclusion is, if achylia is present and gastric cancer or syphilis can be excluded, then look elsewhere than to the stomach for the cause of the pain.

The association of achylia with diarrhea has been emphasized by various authors. In our series of 158, 12 cases complained of diarrhea. Mucous colitis was present twice only. Stockton ("Oxford Medicine," iii, 240) may be quoted as follows:

"Diarrhea is often induced in achylia gastrica, in which disease the stomach frequently empties itself in a precipitate manner, and the undue peristalsis in the

small intestine which follows this is carried over into the large intestine, sometimes as a true peristaltic rush, giving rise to the postprandial diarrhea with lienteric stools. For the reason that constipation occurs in a proportion of cases of achylia gastrica, the frequency with which diarrhea exists is overlooked by many writers. Dudley Roberts, in a careful study of the subject, thinks that in achylia gastrica there is usually to be found some especial reason for the occurrence of the diarrhea. It must be admitted that such special reasons do exist in cases of achylia gastrica, as in other individuals, but I must hold to the position taken that there is something in achylia gastrica which predisposes to diarrhea."

The rapid expulsion of the barium meal with intestinal hypermotility may thus find a rational explanation if the roentgenologist is enabled to interpret his *x*-ray finding in conjunction with the laboratory sheet.

The association of syphilis with achylia is seen when this disease attacks the stomach. Here syphilis and cancer are indistinguishable by clinical, laboratory or roentgen-ray methods. Exploratory laparotomy is equally helpless as a diagnostic measure. The four-plus Wassermann does not exclude cancer. The therapeutic test should, we believe, be applied in all cases which are not proven to be carcinoma by the pathological examination of material removed at operation.

When achylia is present the roentgenologist will do well to include the chest in his examination. In our series, 22 showed disease of the circulatory system and 8 revealed tuberculosis. The teeth also should be rayed in all achylias. In 25 of our series dental sepsis was recorded, but in many of the other cases the teeth had previously received attention, so that the incident of dental sepsis is not well shown in this analysis.

Weakness is a prominent symptom which was present in 45 of our cases, and in all of the 17 cases of pernicious anemia which are included in our series of achylia gastrica. A case of pernicious anemia with abdominal pain presents not infrequently a clinical picture of gastric cancer. The blood findings of cancer may sometimes show a striking similarity to those of pernicious anemia. For this reason the roentgenologist is often called upon to differentiate between these two diseases. If the achylia type of gastric peristalsis has been studied, it will very effectively confirm the absence of a filling defect, and give added assurance to the roentgen-ray interpretation.

Gastroptosis is frequently present with a general loss of muscular vigor. In such cases six-hour residues cannot be interpreted as evidence of gastric ulcer. Gastroenteroptosis is so frequent without symptoms in the average run of all kinds of cases that we have ceased to record them excepting in very aggravated cases, and cannot therefore give figures.

One of the most important aspects of achylia in roentgenological practice is its mimicry of the behavior of the stomach in duodenal ulcer. The duodenal and the achylia type of gastric peristalsis may often be indistinguishable. Very commonly four or five peristaltic contractions may be seen to be simultaneous. The acid control of the pylorus is of course in abeyance in achylia. This, in connection with the rapid expulsion of stomach contents and the often incomplete filling of the duodenal bulb due to the rapid passage of the barium, may appear to give the symptom-complex and the bulbar deformity of ulcer of the duodenum. It is here that the constancy of the deformity and the necessity of serial plates are most to be emphasized. But Carman and others have shown that bulbar deformity is not always necessary for the diagnosis of duodenal ulcer.

If in a given case the history of epigastric hunger pain relieved by eating is found, then a diagnosis of duodenal ulcer would seem reasonable. But in the presence of achylia gastrica, beware of such a diagnosis. If the stomach contents show a total absence of free hydrochloric acid, then the roentgenologist should never make the diagnosis of duodenal ulcer without doubly proving the persistence of a characteristic deformity of the duodenal bulb, and then excluding adhesions, pressure or reflex spasm as a cause of the deformity. In our series, as already stated, no case of gastric or duodenal ulcer was demonstrated.

Without exhausting the subject, we hope that enough has been said to show the advantage of recognizing achylia gastrica in roentgen-ray interpretations of gastrointestinal findings. Another series of cases would likely give different figures. Achylia is associated with such an extraordinary range of pathological states that only very large series of cases could give anything like uniform footings. The frequency of achylia in patients over fifty must result in the inclusion of many pathological conditions that have no necessary relation whatever with the achylia itself. We claim nothing therefore, for our figures excepting to show in a general way from personal experience the roentgenological aspects of this interesting secretory disorder of the stomach.

DISCUSSION

DR. MURPHY. I would like to ask Dr. Crane if he has ever considered achylia gastrica as the first stage of pernicious anemia, and, if he has followed his cases, how many cases of achylia gastrica so diagnosed have been found later to be pernicious anemia.

DR. HICKEY. I would like to ask if he found any difference in the observations between duodenal ulcer and achylia gastrica. He said the differentiation could be made.

DR. CRANE (closing discussion). I think that pernicious anemia is invariably associated with achylia. So far as I know there is a uniformity of opinion among authorities on that point, but that all cases of achylia gastrica ultimately become cases of pernicious anemia I am sure is not true.

Dr. Hickey's question is important for roentgenologists. I do not believe there is sufficient distinction between the hyperperistalsis seen in achylia and the hyperperistalsis seen in duodenal ulcer, so that one could base a conclusion on this point. That is one of the most disturbing features of roentgenological diagnosis of duodenal ulcer. If the roentgenologist does not know whether there is a hyperacidity or an achylia present, he is greatly hampered.

TECHNICAL AND CLINICAL ASPECTS OF THE NEW DEEP ROENTGENOTHERAPY*

BY JAMES T. CASE, M.D., F.A.C.S.

From the Surgical Department of the Battle Creek Sanitarium

BATTLE CREEK, MICHIGAN

ONCE again we find ourselves discussing the "new" roentgenotherapy! How many times those of us older in this *x*-ray work recall discussions of so-called new treatment methods! On each occasion the appellation "new" has been more or less justified by the introduction of some new phase in the technique, such as new filter material, new ideas of crossfire or multiple field irradiation, shorter target-skin distance, or increase of voltage. On this occasion we believe the term "new" is more than ever justified, for we have been equipped with a wealth of new information concerning the physical and biological factors underlying the principles of therapeutic *x*-ray applications, especially regarding the behavior of scattered radiation, which for the first time in the history of roentgenology enables us to feel the assurance of a reasonable degree of precision in dosage.

The various factors referred to have been discussed by the other speakers in this symposium. Permit a word of emphasis on the necessity of *knowing* the approximate wave-length of the rays available, of understanding the rationale of filtration, choice of size, and number of fields, and the target-skin distance from which the application is to be made. It is very encouraging to realize the vast extent of the experimental, physical and biological investigations which have been successfully and accurately carried out by Coolidge, Duane, Shearer, Bovee, Wood, Kroenig,

* Read at the Midwinter Meeting of the Eastern Section of THE AMERICAN ROENTGEN RAY SOCIETY, Atlantic City, N. J., January 28, 1922.

Christen, Dessauer, Friedrich, Seitz, Wintz, and especially by a group of French investigators, including Regaud, Nogier, Béclère, Ledoux-Lebard and their associates. We are further spurred on to renewed effort by the reports coming to us of the practical results secured in the clinics of Europe, especially in Germany, France, and Scandinavia. A number of us have journeyed across the sea to ascertain for ourselves whether or not these reports have been trustworthy; and we find that even though some of them are undoubtedly highly tinged with overenthusiasm, there remain enough cold facts—indisputable tangible results,—to shake the reserve of the most skeptical. Your essayist went to Germany in the fall of 1921, not entirely unacquainted with the immediate results to be obtained with the therapeutic application of *x*-rays produced at 180 to 200 kv., having been provided for nearly a year with equipment to work at this tension. He was prepared to find what he did find, namely, that the new method of deep therapy gives more constant and more pronounced immediate palliation in a larger percentage of cancer cases, and, with some, complete disappearance of signs and symptoms of the disease, concerning which more will be said later. New fields have been opened up in the treatment of a number of benign pathological states which have hitherto not been attacked.

In our discussion we will assume that all are agreed as to the rationality of employing a combination of radium and roentgen-ray therapy wherever the situation of the pathological lesion permits. In this hour's discussion we will be more especially interested in the treatment of malignancy.

SELECTION AND PREPARATION OF CASES

Selection may be made according to the pathological classification of malignancy, but in our present stage we should not stick to this. It is probably wise to exclude from this new deep therapy, at least for the present, those patients whose malignancy has progressed to the stage of advanced cachexia and utter hopelessness, with extensive metastases in bone, liver or lung. In such, the application of the massive doses involved in the new method will very likely hasten the inevitable, and will thus tend to bring unfair discredit upon the radiologist. We may well follow the plan of classifying our cancer cases as (1) early operable (2) fairly well advanced, yet operable (3) inoperable (4) hopeless.

Your essayist is not yet prepared to agree with the pronouncement of some of the German authorities (Seitz and Wintz, Opitz and others) who have abandoned entirely the operative treatment of uterine cancer, still holding with the majority that we should continue to operate distinctly operable cases, combining with our surgery such radiation treatment as may seem appropriate. In our estimation, the pre-operative treatment is of even greater importance than the postoperative, the irradiated cells being in such degree and manner influenced by the treatment that there is certainly less danger of transplantation during the surgical interference.

Just as there is apparently a favorable time for the surgical intervention, there is probably a favorable phase in the development of malignant disease in which application of a massive dose of short wave-length rays will exert a maximum beneficial influence. We must look to the workers in the biological field for selecting the time of application unless we continue to begin as early as possible.

We do, however, have an opportunity for aiding the patient by establishing a plan of preparation for the deep therapy. We look upon the administration of the complete massive dose planned for a given case, given, as we recommend, as nearly as possible in one sèance, as a procedure quite analogous to a surgical operation; and we prepare our patient just as for a major surgical procedure, this preparation involving preliminary rest in bed, attention to eliminative processes, dietary regulation, blood and urine examination, and even a blood transfusion, if it is the type of case in which such a procedure would be considered if the patient were going through a surgical operation. Plenty of fluid should be introduced by the mouth, and if necessary, by retained enemas or by intravenous injection. Lactose or glucose with alkalies may be added to the liquid with advantage.

The patient should come to the treatment room with an empty stomach. It is our custom to administer hypodermically a quarter grain dose of morphine just before starting the treatment; we thereby seem to decrease materially the tendency to nausea and vomiting, and we enable the patient to remain tranquil during the tedious and often uncomfortable treatment.

PLAN OF ATTACK

No two cases are quite alike, either in the distribution of the existing lesion or in the probable line of extension. They differ also in the position and physical dimensions of the zone to which we wish to deliver what we believe to be 10 or 20 per cent more than a definite skin erythema dose of homogeneous and widely but evenly distributed radiation. By careful examination, and by applying our knowledge of the paths along which the lesion is likely to spread, we may prepare a sort of military map and determine in advance with reasonable accuracy what percentage of a definite skin erythema dose to apply through a certain number of definitely defined ports of entry having certain dimensions.

We recognize that there are probably numerous errors in the charts prepared by Dessauer and by Holfelder; yet, in the absence of anything better, we feel that these charts present the best available means of planning our fields and the percentage of the skin erythema dose to be administered through each one. We further recognize the probable great danger in talking of a "carcinoma" or "sarcoma dose," but until we have been furnished with a better basis, we are working on the principles laid down by Seitz and Wintz.

The object of our attack is to deliver to the zone under fire approximately 120 per cent of a skin erythema dose for carcinoma, and 70 per cent of the skin dose for sarcoma, this dose to consist of homogeneous radiation equally distributed to all the pathological or suspected tissues at one sitting. There is considerable discussion as to the necessity of getting this dosage into the tissues at one sèance, and as to just what is meant by one sèance. In our practice, we seldom deliver the dose in one day, but more often within two or three consecutive days, with an added day for the radium application. Regaud and his associates at the Radium Institute in Paris believe it preferable to consume from four to eight days for the administration.

TECHNIQUE OF APPLICATION

In the treatment of uterine carcinoma we employ four areas of *x*-ray application in addition to the intrauterine and vaginal radium treatment. The proportion of the skin erythema dose given through each of the four portals of *x*-ray treatment depends upon the distribution of the lesion and the external measurements of the pelvis. The anterior and posterior areas are large, measuring 16 to 20 cm. square; the lateral areas are smaller. A filter of 1 mm. of copper is used, though it seems likely that less is sufficient, and permits considerable saving in time. We use a target-skin distance of 50 cm. in our pelvic work. For the treatment of breast, neck, jaw and face malignancy we hold that a target-skin distance of 75 cm. is preferable to a shorter distance. Only the question of undue prolongation of time required to administer the necessary dosage deters us from employing a still greater target-skin distance, for these relatively superficial lesions. At present, 8 ma. is the maximum our tubes are thought to be able to stand, and even this intensity keeps the target at what seems at first glance a disconcerting heat. We eagerly await the perfection of some cooling device which will permit the employment of more current, thus shortening the treatments which are no less tedious to the operator than to the patient. Under our working conditions we require 800 ma. minutes, working at 200 kv., with 8 ma. through the tube, at 50 cm. target-skin distance, with the filter and size fields above named, to produce a mild erythema on the skin of the neck; namely, immediately after the treatment a reddening of the skin, followed in about three weeks by a definite light brown discoloration, which later becomes more marked. It is generally recognized that the skin of various portions of the body differs somewhat in

its sensitivity to the irradiation, the most sensitive being the skin of the neck, while the abdomen, thigh, back and face are more resistant in the order named.

In our estimation, it is important to complete the introduction of the entire dose within the shortest reasonable time, for thus does the procedure seem most nearly to approach the surgical ideal. Certainly one has little likelihood of accomplishing anything like as much toward the destruction of the disease at any subsequent attack as at the first one. This does not mean that we do not re-ray our cases; we frequently do. But if the first grand attack has not produced results within six or eight weeks, it is not likely that any subsequent offensive will prove effective. Gaylord has mentioned the period of latency which some patients seem to show before manifesting the good results of treatment, and he feels that three months should elapse before repeating a dose which really merits the term "massive."

It is only fair to describe the technique of others. The Freiburg school lays greatest stress on the single massive dose plan, employing through each of two large fields, one suprapubic and one sacral, at 50 cm. distance, a dose which in thin patients is just short of the skin erythema dose, and considerably exceeds this measurement in fat patients. Here too, radium is used internally to supplement the treatment with *x*-rays. The available statistics from the carefully worked-up material of the Freiburg Frauenklinik indicates that at least a third of the inoperable but not yet cachectic cases of uterine carcinoma are alive and symptom-free after two years.

Just as encouraging statistics are furnished from Erlangen, where an essentially different technique is employed. Here the pelvis is divided into three zones: The first concerns the uterus itself, which is treated at 35 cm. through six (in fat patients, seven) 6×8 cm. portals, three (or four) anteriorly and three posteriorly, all aimed at the seat of the primary tumor, in the belief that about 20 per cent of the skin dose reaches a point 10 cm. below the skin; thus delivering at the site of the disease a total of 120 per cent of the skin erythema dose. After six weeks, during which the skin and the blood picture have recovered, the right parametrium is attacked, again through the six small portals, all laid out to the right of the midline, three anterior and three posterior. After a further six or eight weeks the left parametrium is attacked in a similar manner. The left side is left to the last on account of the high degree of sensitivity of the rectosigmoidal mucosa. By thus planning the treatment, the rectum and lower sigmoid, which usually lie more to the left than to the right side of the pelvis, are allowed twelve to fourteen weeks to recover from the irritation following the treatment of the primary tumor, before receiving the second irritating dose to which they are subjected during the treatment of the left side of the pelvis. If the left parametrium is more involved than the right, then the danger of overirritating the rectal mucosa must be faced.

The Erlangen school also recommends the employment of the large field, longer distance technique when there is widespread diffusion of the disease throughout the pelvis, especially in dealing with sarcoma. Since Professor Seitz has moved to Frankfort, he has introduced the above technique into the Frankfort Frauenklinik, where it is faithfully carried out.

It is of the utmost importance to assure the presence of the filter. In the past, with the treatment methods usually in vogue throughout the United States, the omission of the 3 or 4 mm. of aluminum used as filter has resulted in acute lesions exceedingly distressing alike to patient and operator; it is not difficult to picture the unfortunate result if an omission of filter occurs in the course of treatment with the new technique. Various methods of assuring the presence of the filter have been devised. The use of some one of the ionometers will betray at once the omission of the filter by the rapid discharge of the electroscope. The plan carried out in our clinic seems worthy of recommendation. The operator of the treatment instrument has strict instruction not to turn on the current until the voltage, the target-skin distance, the protective coverings and the filter have been verified by one of the physicians of the

department who is required to sign his initials personally in the blank provided for that purpose.

DOSAGE

As above intimated, the dosage administered is intended to approximate as accurately as possible, 120 per cent of the skin erythema dose for carcinoma, and 80 to 85 per cent of this dose for sarcoma. Whether the skin dose is estimated by some method of ionometry, it transpires sooner or later that the individual installation under the peculiar working conditions of each laboratory will become standardized, and the chief dependence will be placed on the reproduction of the six physical factors (voltage, milliampèrage through the tube, time of application, filter, target-skin distance, and size of field of entry) rather than upon the electroscopic readings. For the present at least, the use of the ionometer in the average American's practice will be greatest for the instruction of the physician and his office personnel, and for experimental investigations.

PROTECTION OF THE PATIENT

Our tube enclosure is not at all satisfactory; therefore we feel bound to cover the patient with protective material, except for the opening through which he is being treated. Lead or lead-rubber protective material, grounded to the steam or water pipes, is supported on hoops or other frame work to relieve the patient of unnecessary weight. The protection for the head and face may be so arranged as to permit the freedom of the patient's arms to hold a book or magazine. Enough blankets are provided to keep the patient warm, thus permitting free ventilation of the room with fresh air even in the coldest weather. In some instances a retention catheter is placed in the bladder to avoid the necessity of disarranging the protective material before the conclusion of the treatment. Only a physician is permitted to arrange the area under treatment and the protective material, and to verify the presence of the filter, the correctness of the voltage and other treatment factors, and in our clinic he is required to certify to the performance of this duty by initialing the book.

IMMEDIATE EFFECTS

During the treatment the patients frequently become nauseated, and many of them vomit. Morphine minimizes this tendency and lessens complaint as to discomfort. When treating the glands of the neck, the axilla or the groin, the application is promptly followed by an immediate swelling and reddening of the area treated, so marked that unless the patients are warned in advance, they are apt to call for the attending physician six to twelve hours after the application, alarmed by the occurrence. In another twelve to twenty-four hours the visible swelling has disappeared, but the discomfort continues for several days to a greater or less extent. In general, there is a primary blush or reddening noted on the skin lasting one or two days, followed in a week or ten days by the deeper reddening of the erythema, marking a full erythema dose. The reddening gradually fades and is later replaced by a brown discoloration of the skin. If the treatment has been given in a very much larger dose, it is possible to observe a final whitening of the skin owing to destruction of the function of the pigment cells.

Following treatment in full dose for malignancy of the lip, tongue, tonsil, thyroid, supraclavicular or mediastinal glands, or any type of malignance involving intensive radiation to the chest or neck, patients frequently complain of temporary dysphagia, dyspnea, dry cough, disturbance of voice at times approaching aphonia, pharyngeal irritation simulating pharyngitis or tonsillitis, edematous reddening of the uvula, pillars and pharynx—all, however, without the constitutional symptoms of an acute infection. These symptoms usually pass away in four to ten days.

Much has been said in this country regarding blood changes of a serious nature following the new deep therapy. We have been given to understand that it is not infrequently necessary to administer a blood transfusion to counteract the

depressant effect of the treatment on the blood-forming functions. Our experience and observation do not confirm this impression. In very marked cases of leucopenia it is true, such transfusions may become justifiable, but experience has shown that when the patient is already cachectic, the prospect of help from the irradiation is remote, if, indeed, the contrary result is not substituted. The immediate effect of a heavy treatment is a transitory rise of the white count of, say, from 7,000 to 10,000 or 12,000, within a few hours, followed by a gradual rise in the white count, until at the end of from four to eight weeks it has returned to about normal. There is very little change in the number of erythrocytes, a fall of 4 or 5 per cent being the maximum change noted in any of our cases. Abnormal cell elements are not especially numerous. In going over the protocols of a number of cases observed, we may note the following with reference to three typical cases:

	Case A	Case B	Case C
Before.....	4,312,000	4,630,000	3,508,000
At once after....	210,000	4,400,000	3,220,000
6 hours.....	4,120,000	4,300,000	3,110,000
3 days.....	4,100,000	4,500,000	3,400,000
6 weeks.....	4,280,000	4,580,000	3,600,000

and the following with reference to white cells in the same cases:

Before.....	5,300	4,300	5,800
Im. after.....	5,100	3,800	4,600
6 hours.....	5,000	3,400	4,000
3 days.....	4,900	3,300	4,700
6 weeks.....	5,200	4,000	5,500

In none of the above patients was the hemoglobin lower at the end of the six weeks of observation than at the beginning.

In other words, there appears to be no permanent deleterious effect upon the blood-count resulting from the massive doses. In a limited number of observations the blood-sugar has been moderately lowered and the blood-nitrogen slightly elevated. We have not marked any constant change in the coagulation time of the blood. The diminished blood-sugar could easily be explained by the lessened alimentary intake during and immediately following the treatment.

Rectal and bladder tenesmus are fairly constant sequels to pelvic irradiation in massive doses. This seems best relieved by radiant heat applied locally, warm sitz baths, and sedative drugs. In one of the German clinics we saw a special device for the application of incandescent light treatment within the vagina. The daily bowel movements begin to increase in number on about the third day reaching ten to fifteen in twenty-four hours by the eighth or ninth day, then gradually returning to normal at about the same rate.

"Roentgen intoxication" is one of the less serious complications of the newer deep therapy, though it stands out as one of the most disturbing to the patient. Headache, nausea, vomiting and weakness are fairly common in a greater or less degree, but fortunately the symptoms are transient and usually disappear with forty-eight hours. Many patients suffer during the first application of the series when the areas are treated on successive days, and are not at all inconvenienced during the remaining two or more days constituting the session. It is impossible to foretell who will be sick. Some go through the whole session without inconvenience, while others, appearing equally able to withstand minor symptoms are wofully upset for a day or two. Occasionally (especially after long-distance irradiation in breast cases) the roentgen sickness lasts for weeks and is very disturbing to the patient, though, after all, of minor consequence compared to the malady for which we treat. Various theories have been advanced to explain the intoxication, for such it seems to be,—disturbance of the internal secretion of the ovaries, the adrenals, or other glands of internal secretion; toxins developed in the intestine, especially the small intestine; disturbance of the sympathetics; acidosis; vitiation of the air of the room; absorption of products of disintegration of the tissue under radiation; changes in the blood (Heinecke). To all of these suggestions one immediately thinks of exceptions; attention to any one fails to do more than slightly lessen the discomfort.

One naturally chooses for treatment work a room with a high ceiling, well ventilated; he adopts a system of high tension wiring which minimizes corona; he puts his current-generating apparatus

in another room; he encourages the patient's eliminative processes in every possible manner; sedative drugs are employed to minimize the nervous or psychic factors (and these latter are of no mean importance); certain endocrine therapy may prove useful. The ordinary tests for acidosis (estimation of the CO_2 tension of the aveolar air, study of the urine and the chemical analysis of the blood) in our clinic have failed to show evidence of acidosis even in cases subjected to the largest doses we have dared to administer, or in patients exhibiting the most distressing symptoms of irradiation sickness.

RESULTS

The immediate reaction upon the disease is very encouraging. In a given series of consecutive cases (excluding the cachectics) one sees a larger number of more prompt improvements. Pain is usually relieved; bloody and purulent discharges lessen or disappear; the general condition of the patient is improved in a considerable proportion of cases. Some have responded no better than before, but the sum total of our conclusion is that palliative results have appeared more promptly than ever in a larger percentage of cases, while in a few, the visible evidences of the disease have disappeared. We have no right yet to talk of permanent results, but we do feel justified, from our own experience, in expressing the encouragement we feel in going earnestly ahead with our work.

Personal investigation of the good reports of apparent cures from Germany revealed a somewhat modified tone of optimism. Reports published in American medical journals give figures of apparent cure after two or three years approximating 60 or 70 per cent. Actual investigation of the figures given today in the leading clinics showed the most optimistic to claim only 30 to 35 per cent. The most bitter critics of the overenthusiastic admitted perhaps 15 per cent of apparent cures in inoperable cases! Our German colleagues have been carrying out this treatment for four or five years, and they have small series of cases now alive three years after massive treatment with what they consider nearly ideal technique. Several well-known gynecologists have abandoned the operative treatment of cancer of the uterus in any stage, submitting even their earliest cases to the combined radium and *x*-ray treatment. Everywhere was found a reluctance to talk with much enthusiasm until another two years or more have passed by. We shall do well to follow this example.

REPETITION OF TREATMENT

We believe an interval of from six to twelve weeks should elapse between treatments given in the manner earlier described in this paper. In some cases where the first series of treatments failed to produce a definite reddening of the skin, the urgency of the situation has led us to give a supplementary dose within two weeks. We have been fearful of late-appearing damage to the skin, but in none of our own cases have we ever seen this. A herpetiform skin eruption has followed within a week or two in a rather striking number of cases; in half a dozen breast cases, this rash has seemed to be a true herpes zoster. In one patient, it appeared twice, each time following a treatment. In no instance have we continued the treatment after the third massive application. In the European clinics we saw a few instances of the so-called chronic indurative edema which occasionally appears in the treated area several weeks after repeated application. The appearance of this induration should be a warning to discontinue the roentgen therapy through the area involved, for it seems that it is in just this kind of situation that the late skin injuries have appeared. Even so, the number of recorded cases of late skin damage is very small. Seitz admitted only two such cases, and in one of them it is likely that the late damage would not have appeared had not the area been subjected to chemical irritation due to the patient's occupation.

CONCLUSIONS

We should accept with considerable reserve the reports of clinical results from the work of our European colleagues, but we should welcome gratefully the enormous

fund of information concerning the physical and biological basis of deep therapy furnished by them and by our American investigators which will enable us to make most intelligent use of the shorter wavelength roentgen radiation. A definite advance has been made in deep radiotherapy. Unprecedented good results (of at least temporary duration) are being secured in a more constant fashion in a larger percentage of patients presented for therapy. I believe we should discard our old methods just as rapidly as we are equipped, not only with apparatus, but especially by a familiarity with the principles underlying the new method. Radium therapy will be more than ever successful in gynecological malignancies when combined with the intelligent application of the new, more penetrating *x*-rays, which by their adaptability to conversion into practically homogeneous radiation, will supplement the internal use of radium in a manner best calculated to reach the lymphatic lines along which extension of the malignant disease occurs. For benign lesions of the pelvis, for which radiation is indicated, it cannot be stated that the newer, high voltage apparatus is a necessity; but it is certainly a great convenience.

X-RAY AND CLINICAL FINDINGS IN THE NORMAL CHEST (CHILDREN SIX TO TEN YEARS OF AGE)

NATIONAL TUBERCULOSIS ASSOCIATION
MEDICAL RESEARCH

THE National Tuberculosis Association some time ago began a new and important phase of its work in an attempt to increase the quantity and character of research work in problems related to its own field in the United States. For this purpose it appropriated $20,000.00 and appointed a small committee composed of Dr. Wm. Charles White, Medical Director of the Tuberculosis League of Pittsburgh, Dr. Paul A. Lewis, Director of Laboratories of the Phipps Institute, Philadelphia, and Dr. Allen K. Krause, Director of Kenneth Dows Research Fund, Johns Hopkins Hospital, to expend these funds to the greatest advantage.

This committee decided that the best use of these funds would be in assisting researches already under way that held the greatest promise of increasing the practical knowledge of physicians dealing with tuberculosis. This, they considered, would bring the greatest help to those suffering from tuberculosis and the greatest boon to the public from whom the funds were collected. This plan has been carried out in cooperation with the universities.

One of the researches was an effort to establish the *x*-ray and clinical findings in the chest of a normal child up to ten years of age. For this problem the National Tuberculosis Association nominated the following groups of roentgenologists and clinicians.

Dr. H. K. Pancoast and Dr. H. R. M. Landis—University of Pennsylvania.

Dr. F. H. Baetjer and Dr. C. R. Austrian —Johns Hopkins University.

Dr. H. K. Dunham and Dr. K. D. Blackfan—University of Cincinnati.

The signed reports of these physicians are here presented in two sections with the hope that they may promote a discussion which will be fruitful in establishing the truth in these two fields.

THE X-RAY AND CLINICAL FINDINGS IN THE NORMAL CHEST OF THE CHILD

Report of the Clinical Division of the Committee on Medical Research of the National Tuberculosis Association.

The value of roentgenography in determining the presence of pulmonary disease has long been recognized. Studies to

determine the roentgenograms of various pathological lesions of the lung have been almost without number, yet much difference of opinion exists in the interpretation of findings, largely because no satisfactory observations have been made establishing the variations that may occur in the normal. To one observer, shadows noted are indicative of disease; to another, they are not evidence of a pathological process. To one, they represent lesions of clinical significance; to another, they suggest changes of no moment. The realization of this unsatisfactory state of affairs was widespread, but it remained for the Research Committee of the National Tuberculosis Association seriously to consider it and to set about to correct the shortcomings.

In the spring of 1920, that Committee called together the collaborators in this work and instructed them to set about in ways of their own choosing to solve the problem, extended to them a financial grant, and, in order that the problem might be a very definite one, asked that the immediate study be limited to a consideration of the chests of normal children between the ages of 6 and 10 years. The work was begun promptly and a preliminary report was made at the annual meeting of the Association in May, 1921. The findings at that time were incomplete, and because of the then limited observations, no very definite conclusions were drawn. However, the practical need of a solution of the problem was apparent. Study was continued throughout 1921 and the first four months of 1922, and the data independently assembled were jointly discussed to evaluate them. Although each pair of workers carried on its investigations without inter-group consultation, although each approached the subject from a different angle and when first met held views apparently not altogether in accord, it was agreeable to find that an exchange of conclusions disclosed almost an unanimity of opinion. The findings of these six observers—three clinicians and three roentgenologists—are presented to you for consideration:

Theoretically, the normal child is one of ideal height, weight and development for his age, without subjective or objective evidences of deformity or of disease, and without residual changes due to antecedent pathological processes. Practically, a normal child is one of average height, weight and development for his age, symptom-free and without signs of disease. Each such individual, in more or less relation to his age, will have been ill more or less often, and as a consequence may be expected to show variations from the ideal, not because of present disease, but as a result of residual changes that persist. An appreciation of these facts makes it apparent that the findings, clinical and roentgenographic, in normal children as we meet them will vary greatly from any fixed standards, and still must be considered as variants of normal.

The clinical data dealt with in this report were obtained by careful examination of apparently healthy children between the ages of 6 and 10 years. All children who showed signs of disease were excluded from the series. Individuals from various strata of society, foreign and native born, residents of urban and of rural communities, school children and children residing in institutions, children exposed to tuberculosis and some without a history of such exposure, children with and without a history of previous infectious diseases, all symptom-free, and of an approximately normal height and weight for their ages, were studied. A history of each individual was recorded, and in making the examinations of the chest, care was always observed to have the child relaxed and to see that no cramped or unnatural posture was assumed, for, as is well known, faulty position may lead to findings that cause confusion in interpretation. In addition, a tuberculin test was made on every child. The clinical data were then assembled and after the roentgenologist had interpreted his plate independently, the clinical and roentgenographic findings were correlated.

In all, over 500 children were thus studied, and as a result some definite conclusions seem warranted.

As in the adult, so in the child, vocal fremitus is more marked over the right upper chest than over the left.

It is generally stated that the percussion

note elicited over the lungs of normal children within the age limits under consideration is fuller, more tympanitic, of higher pitch and more resilient than that noted over those of adults, and that frequently the tympanitic quality is quite outspoken, especially over the lower lobe of the left lung. Although in general our observations confirmed this view, we have been impressed by the fact that in an appreciable number of such children, the note obtained on percussion over the lungs is indistinguishable in quality from that elicited over the lungs of normal adults and that the usual resilience of the note is lacking. These findings in many instances have an analogue in shadows noted in the *x*-ray films, shadows indicative of increased density along the bronchial tree, similar to those seen in the plates of normal adults. This correlation of the findings on physical examination and on *x*-ray study is more constantly possible in studies of the upper half of the chest. When minor changes, similar to those discovered by *x*-ray examination of the upper lobes, occur in the bases, they usually escape detection on physical examination. In those instances in which no shadow is found to explain the deviation of the note from the generally accepted one, it is our belief that the lack of resilient quality may be due to a decreased elasticity of the chest wall.

The so-called tympanitic quality of the percussion note over the left base may be increased, decreased or be entirely lacking, depending upon the degree of distention of the stomach or colon, and the curvature of the spine, and may likewise vary with the position of the diaphragm or with the posture of the child during the examination. The note over the upper thorax is often the same on the two sides. Kronig's Isthmus averages 5 to 6.5 cm. in width. The lower margins of the lungs posteriorly are at the level of the 10th or 11th rib and descend from 1.5 to 3.5 cm. during forced inspiration.

A just detectable diminution of resonance over the apical regions is of no significance unless associated with a modification of the breath sounds in those areas, or with other abnormal ausculatory findings.

It is generally accepted that normally in childhood, the breath sounds have a harsh, sharp character, with expiration longer and better heard than in the normal adult. This so-called puerile breathing is physiological, and though it may seem trite, let it be emphasized that this exaggerated vesiculo bronchial respiratory murmur, especially well heard in the areas overlying the great bronchi (i.e. anteriorly at the level of the first interspace and the second rib just lateral from the sternal margins, and posteriorly, particularly on the right side, at the level of the second to the fourth spine) is often incorrectly interpreted as evidence of pulmonary disease. An auscultatory finding that has not been pointed out, or, at least, has not been emphasized, has come forcibly to our attention in carrying out this study. Just as the full, deep note or higher pitch characteristically elicited by percussion of the child's chest is often replaced in health by a note more like that produced when one percusses the normal chest of an adult, so, on auscultation of a child's normal lungs, the exaggerated or puerile breath sounds may be lacking, and instead, the so-called vesicular respiratory murmur characteristically present in adult life is heard. This finding, regarded by us as a physiological variation, has been noted as early as the age of four years and may perhaps occur in younger children. It is more readily appreciated and more often found than the variation in the percussion note just described. In more than 50 per cent of the children in which this type of breathing was heard, examination with the *x*-rays gave findings like those obtained by a study of normal adult chests. In fact, the agreement of clinician and roentgenologist was so constant that we have come on the basis of these variations to designate the chest of normal children as of "puerile" or of "adult" type. The essential fact to be stressed is that so-called vesicular respiration is heard with great frequency in normal children, and is to be regarded as a variation of normal and not necessarily as an indication of disease.

These variations and those of the percussion note are more generally found in children with a history of infections of the respiratory tract. No satisfactory

explanation for this finding is offered. It may be due in part to altered resilience of the chest wall, a suggestion supported by the fact that in some instances in which it was noted, diminished elasticity of the thoracic wall was apparent on percussion. It may stand in relation to variations of elasticity of the parenchyma of the lung. It may be due to a relative narrowing of the lumen of the bronchial tree. It is hardly to be considered evidence of increased density of respiratory tissue, for, theoretically, at least, that should lead to a modification towards bronchial breathing.

Concerning the whispered voice sounds, little comment needs to be made other than to emphasize their loud transmission often with syllabation over the region of the major bronchi. Auscultation of these sounds over the upper thoracic spine of the children has led to the conclusion that D'Espine's sign as indicative of enlarged tracheobronchial lymph-nodes is, to say the least, of doubtful value. In 23 of the children, this sign was elicited without other signs of a mediastinal mass and without any corroborative evidence on *x*-ray examination. In 3, the sign could not be elicited, although from the *x*-ray plate it might have been inferred that it should be. Eustace-Smith's sign is so generally present in normal children that it is of little or no practical diagnostic worth. The presence of these two signs together with impairment of resonance in the interscapular region is all too frequently made the premise for a diagnosis of tuberculosis of the tracheobronchial lymph-nodes. This is unwarranted, for, as indicated, these signs are unreliable evidence of a pathological condition, and the determination of a diminution of resonance in the interscapular region requires such a nicety of technique that even masters of percussion disagree as to the presence or absence of significant findings in this region of the chest.

A year ago, in the preliminary communication to this Association, we stressed the importance of the rôle that antecedent infections might play in the production of areas of increased density within the respiratory tract (bronchial tree, parenchyma of the lungs, etc.). This fact is re-emphasized, for further study has established the importance of it. Not only may recognized or remembered infections of the bronchi and lungs be responsible for alterations in these tissues, but other diseases not ordinarily considered of significance in this regard may be causal of such changes. For example, our observations indicate that after measles, pertussis or tonsillar infections, areas of increased density radiating from the hilum into the bases especially, occur with great frequency. Such lesions generally are not discoverable on physical examination and would be unsuspected but for the use of the *x*-ray. They are referred to in the clinical part of our joint report in order to point out the need of a careful history as well as examination in all individuals, before proceeding finally to interpret the findings of the roentgenologist. By way of digression, it may be interesting to point out the fact that though measles and pertussis have been known to produce lesions in the upper air passages, involvement of the lower tract has been considered a complication and was thought to occur only when evidence of bronchitis or of bronchopneumonia was discovered. Our observations indicate that there may be a mild inflammatory process throughout the respiratory passages in a large percentage of the so-called uncomplicated cases of these diseases. This suggestion warrants further study in relation not only to the infections under consideration but also other infectious diseases. That such shadows, mediastinal and basal, noted in children who give a history of uncomplicated measles and pertussis are evidences of healed processes is evidenced by the experience that similar shadows of like origin have remained unchanged and without the development of clinical symptoms in a series of children observed from three to five years. Such changes must be properly evaluated as indices, not of present disease, but of lesions past and healed, not as warrant, for the diagnosis of present illness and the institution of treatment, but as scars of infections met and overcome.

Most of the children included in this study were tested with tuberculin—some were given a cutaneous test with old tuber-

culin (Pirquet) others were tested by the intracutaneous method (Craig).

The foregoing facts have been detailed at some length to establish the major thesis that, clinically, the ideal, normal child is a hypothetical impossibility. Children, apparently healthy, symptom-free and active, show, on careful examination, many deviations from fixed standards, variations that must be interpreted as within physiological limits. Standards of height and weight must be elastic, measures of resonance and of resilience of the chest must not be rigid, and estimates of acoustic phenomena must permit of a range of difference from the ideal. These facts, clinical experience establishes beyond peradventure; and they suggest a corollary, namely, that *x*-ray examination of the chests of such children may be expected to show comparable deviations from a fixed ideal roentgenogram.

The studies reported, fortified by past experience, warrant the following conclusions:

1. The data obtained on percussion and auscultation of the lungs of normal children show wide variations from a fixed standard. These variations are usual and are considered to be within normal limits.

2. Inasmuch as the changes referred to are dependent often upon alterations that persist as the residua of past infections of the respiratory tract, it is obvious that a careful anamnesis, with special reference to all infections, is necessary if diagnostic errors are to be avoided. Even a history carefully taken is often unreliable, as minimal infections are soon forgotten by many and among the unintelligent classes even more significant indispositions are not readily recalled.

3. Failure properly to evaluate these deviations from a fixed standard will often lead to the unwarranted diagnosis of disease and to even less justifiable treatment.

4. With a proper appreciation of the widest variations that the normal may present from the ideal, the informed clinician is better able correctly to understand the findings of the roentgenologist, and each, cooperating with the other, is less liable to error.

5. D'Espine's sign as indicative of enlarged tracheobronchial lymph-nodes is of little value.

6. Recognition of and familiarity with the foregoing data is of cardinal and practical importance to every patient, potential and established. Without a proper appreciation of the facts set forth, no intelligent differentiation between a normal and an abnormal respiratory tract can be made.

In brief, to establish the presence or absence of disease, it is imperative that all data—clinical, laboratory and roentgenographic—must be evaluated and correlated, and that no one fraction of the evidence be stressed to the exclusion of the others.

(Signed) C. R. Austrian
H. R. M. Landis
K. D. Blackfan

May 6, 1922.

THE X-RAY AND CLINICAL FINDINGS IN THE NORMAL CHEST OF THE CHILD

Report of the X-Ray Division of the Committee on Medical Research of the National Tuberculosis Association

It is generally conceded that one of the most important factors in accurate interpretation of the appearance of morbid processes in the roentgenogram of the thorax is a thorough familiarity with the normal, and variations therefrom, within normal limits. With a full realization of this in view, the National Tuberculosis Association, in 1920, appointed a committee comprising three roentgenologists and three internists to make a study of the normal chest of the child between the ages of six and ten years. This group was instructed to work in cooperation, and to make a report of their investigations before the Association when their studies were completed and their conclusions reached. The members selected for the committee were Dr. H. Kennon Dunham of Cincinnati, Dr. Frederick H. Baetjer of Baltimore and Dr. Henry K. Pancoast of Philadelphia, to act in the capacity of roentgenologists and to work in cooperation with the respective internists in the same cities, Dr. Kenneth Blackfan, Dr. Charles R. Austrian and Dr. H. R. M. Landis. Each group of two was to work

independently until a satisfactory number of individuals were examined and the entire committee was then to meet and draw their conclusions for presentation. It was to be the duty of the internist in each group by careful clinical study to select as nearly normal children as possible for examination by the roentgenologist. The entire procedure was to be carried out with strict cooperation between the two members of each group.

It was soon realized by the *x*-ray members of the groups that an attempt to describe a normal chest was practically impossible. Their endeavors soon began to centre around the description of a theoretical normal with wide variations that would serve as a basis for the interpretation of abnormal appearances, and tend to preclude the possibility of erroneous diagnoses being based upon faulty interpretations of hilum shadows, trunk shadows and linear markings, more or less altered in appearance by the frequent respiratory infections of children. They realized that herein had existed the greatest source of error in interpretation; and no doubt the Association had this same thought in mind when the committee was appointed to take up these investigations. Errors in interpretation have been made chiefly in connection with the diagnosis of pulmonary tuberculosis.

It was the consensus of opinion that children are probably more apt than adults to show definite *x*-ray evidences in the hilum and trunk shadows of simple as well as serious respiratory infections. Practically all children of the ages of those examined have had at one time or another one or more respiratory infections, especially measles and whooping-cough, that are likely to produce very apparent changes in the shadows mentioned and which will remain distinctly visible for a variable period of time. These apparent deviations from the normal are not necessarily abnormal when observed, but may be the harmless results of one or more infections. No doubt such appearances have many times been misinterpreted as evidences of tuberculosis. In the conclusions reached by the committee, the attempt has been made to preclude this possibility.

Many of the general observations made have not been included in the conclusions. One of those perhaps worth mentioning is the fact that the heart of the child is found to extend relatively further to the right than that of the adult.

The thoroughness with which the studies were carried out may be in part realized from the number of individuals examined. Over five hundred children were selected from all strata of life, as stated in the clinical report of the committee.

The groups comprising the committee met at the Phipps Institute, Philadelphia, March 3, 1922. Prior to this meeting, there were misgivings as to the possibility of an agreement upon any very definite conclusions, but, much to the satisfaction of all the members, a definite agreement was reached, and the conclusions were completed, after a few hours' careful deliberation.

To assist in a better understanding of the conclusions of the committee, a composite diagrammatic reproduction of several roentgenograms was made. It must be remembered that the three zones, like the chest, have thickness as well as length and breadth. Thus the zones extend anteriorly and posteriorly as well as laterally, from the lung root.

CONCLUSIONS OF THE X-RAY DIVISION OF THE COMMITTEE

1. *The Normal Chest.* The normal chest of the child from the roentgenologic standpoint is subject to such wide variations within normal limits as to be beyond the possibility of exact description.

2. *Hilum Shadow.* The conglomerate shadow commonly called the hilum shadow, when found lying entirely within the inner third or zone of the lung area can be disregarded (or regarded as normal) except where it is made up of a solid mass of homogeneous shadow giving undoubted evidence that it represents a growth or mediastinal pleurisy.

3. *Calcified Nodes.* Calcified nodes at the root of the lung, without evidence of lung disease, are of no significance except as a possible evidence of some healed inflammatory condition, possibly,

but not necessarily, tuberculous. They are a common finding in normal chests.

4. *Density and Thickness of Trunk Shadows.* In the normal lung, the bronchial trunk shadows are not visible in the extreme apical regions. For convenience of description, the remainder of the lung is divided into three vertical zones, extending outward from the lateral border of the spinal shadow to the lateral chest border.

The inner zone contains the root shadows.

The mid-zone contains the trunk shadows, gradually fading out into their final subdivisions.

The peripheral zone contains radiating lines from these, fading off before the periphery is reached.

Where in the mid-zone or peripheral zone, these shadows do not disappear in the characteristic fashion described, the appearance may be evidence of a variety of conditions, past or present, of an inflammatory nature or otherwise. It may accompany a tuberculous process, but is not necessarily indicative of tuberculosis.

5. *Improper or Misleading Terms.* The use of the terms "peribronchial tuberculosis" and "parenchyma tuberculosis" is not to be recommended in the interpretation of roentgenograms of the chest. Until corroborated by laboratory or clinical findings, the use of the terms "active" and "quiescent" should not be definitely applied to evident lesions demonstrated on plates.

(Signed) HENRY K. PANCOAST
KENNON DUNHAM
F. H. BAETJER

May 6, 1922.

ROENTGENOGRAPHY OF INTRACRANIAL PASSAGES FOLLOWING SPINAL AIR INJECTIONS

BY CHARLES L. MARTIN, M.D., AND CLAUDE UHLER, M.D.

From the Laboratories of the Baylor Medical School

DALLAS, TEXAS

ANY new procedure related to the brain or spinal cord is approached by most physicians with great caution, and this is undoubtedly as it should be. However, the need of more accurate diagnostic methods in studying intracranial disease is so urgent that every reasonably safe procedure should be given a fair trial.

It may not be out of place to set down some operative statistics in an effort to emphasize this point. Bailey[1] states that out of 118 consecutive cases diagnosed as brain tumor at the Peter Bent Brigham Hospital, 55 were not verified and 31 were found to be suffering from other conditions such as cerebral thrombosis, embolism, syphilitic meningitis, cerebral hemorrhage, meningoencephalitis, multiple sclerosis and posttraumatic psychoses. Ransohoff[2] claims that only about 8 per cent of all brain tumors can be successfully removed at the time of recognition. Heuer and Dandy,[3] in a series of 45 suspected tumors of the cerebral hemispheres, failed to locate the tumors at operation in 44 per cent of the cases. Bruns[4] states that only 3 to 4 per cent of brain-tumor operations are surgical successes. The mortality for such operations done under Victor Horsely at the National Hospital was given by Tooth[5] as 32 per cent. Krause[6] gives the mortality as 50 per cent in 109 operations at the Berlin Clinic. Harvey Cushing[7] states that in 350 operations, the immediate mortality was 10 per cent and the permanent cures 5 per cent. It seems only fair to assume that these figures might be improved materially by the introduction of an efficient method of diagnosis.

The use of air as injection material for the subarachnoid space and ventricular system as advocated by Dandy[8] offers wonderful possibilities. His system of investigation will undoubtedly soon be

accepted by the profession as a fit companion for the barium meal and the pyelogram. Many roentgenologists will remember his original article entitled "Ventriculography following the injection of air into the cerebral ventricles" which appeared in the AMERICAN JOURNAL OF ROENTGENOLOGY in January, 1919. In October, 1919, a second article dealing with the roentgenography of the brain following the injection of air into the spinal canal appeared in the *Annals of Surgery*. It has been our good fortune to have the opportunity of examining a series of 14 cases by this latter method at the Baylor Hospital during the past year. Our results have been, on the whole, very satisfactory and we have had no mishaps.

The technique used has been essentially that recommended by Dandy. The lumbar punctures were done in the roentgen-ray laboratory following the administration of full doses of morphine. The adult patients were required to sit up with the head bent slightly forward during this procedure, and it would seem that this is the ideal position for filling the ventricular system. The children were given a general anesthetic and placed in the right lateral position on a table with the head elevated so that the table top made an angle of about 15° with the floor. A 10 c.c. syringe was fitted to the lumbar puncture needle after its insertion into the spinal canal. Following the removal of each 10 c.c. of spinal fluid, about 9 c.c. of air were forced into the spinal canal. This procedure was continued until no more fluid could be obtained or until at least 40 c.c. of air had been injected. The needle was then removed and a small dressing placed over the puncture. At this point the children were held upright with the heads tipped slightly forward for four or five minutes. All roentgenograms were taken on the inclined table used in doing the punctures on anesthetized patients. Two lateral views, a posteroanterior and an anteroposterior view, were taken in each case. It was also found advisable to take a lateral view before beginning the procedure. This made the identification of suture lines and blood-vessel grooves much easier.

From the patient's point of view the investigation is not altogether pleasant, but the information obtained often far outweighs the importance of the symptoms produced. These symptoms have been quite temporary in our cases. Headache has appeared with each injection, and at times it has been quite severe but all unpleasant symptoms have disappeared within twenty-four hours. In a few cases pain has appeared in the back or in a

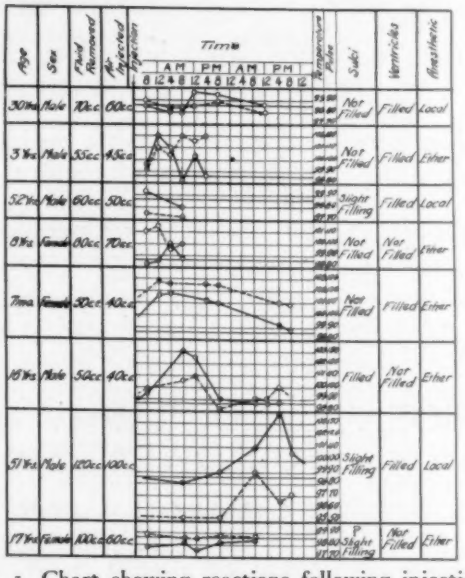


FIG. 1. Chart showing reactions following injections. The solid lines represent temperature and the broken lines the pulse.

leg during the injection; possibly because nerve filaments got caught in the needle. This pain is usually transient. Eight of our patients remained in the hospital for twenty-four hours or longer, and Figure 1 shows the temperature and pulse variations. The solid lines represent temperature and the dotted lines, pulse variations.

No good explanation of the temperature rise can be offered at the present time, but it doubtless has some relation to a disturbance in pressure on the heat center. Since all the patients did not show a marked rise, we feel quite certain that no infectious organisms were introduced with the air. No attempt was made to study the absorption of the injected air except in one case. At the end of six days there was a small amount in the lateral ventricles, although none of the other injected structures could be made out.

A word should be interposed here regarding the selection of cases for this type of injection. The most important contraindication is a brain tumor in the posterior fossa. It is a well-known fact that removal of the spinal fluid in such cases may cause death. The brain stem is pushed into the foramen magnum by the pressure from above, when the pressure in the spinal canal is lowered. Where there is any question of such a condition being present, a ventricular puncture should be done first through a small trephine to

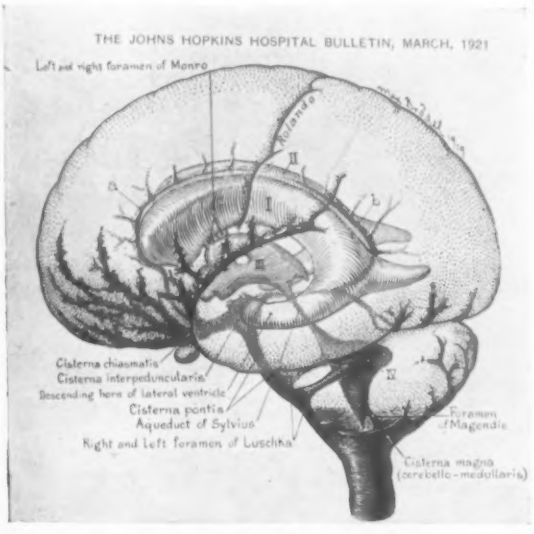


FIG. 2. Drawing made by Max Brodel to show the arrangement of the intracranial spaces.

equalize the pressure on the two sides of the medulla. Infections and hemorrhagic conditions have also been mentioned as contraindications. The method appears to be of the greatest value in studying cases of hydrocephalus where it is of importance to locate definitely the point of obstruction.

In attempting to study the details of the intracranial passages we found the standard textbooks rather unsatisfactory. Since others may experience the same difficulty, a few roentgenograms of normal brains may be worthy of discussion. Figure 2 shows a drawing which appeared in one of Dandy's recent articles. This drawing gives the most graphic representation of the cerebrospinal fluid circulatory system which has come to our attention. According to our present conception, the spinal fluid is formed in the lateral ventricles labelled I and II in the sketch. It passes through the foramen of Monro on each side into the third ventricle and from there down through the long narrow aqueduct of Sylvius into the triangular-shaped fourth ventricle. Three passages, the foramina of Luschka and the foramen of Magendie, carry the fluid into the cisterna magna and the cisterna pontis, both of which communicate with the subarachnoid space of the spinal cord.

FIG. 3. Lateral view of a normal baby's skull made following the injection of air through lumbar puncture. The sulci are not injected. None of the roentgenograms shown are retouched.

The cisterna pontis is continued forward as the cisterna interpeduncularis and the cisterna chiasmatica, and the spinal fluid after having traversed these passages is distributed over the surfaces of the cerebral hemispheres through the branches of the cerebral sulci and is here absorbed. Should an obstruction occur in one of the narrow passages, that is, in the aqueduct of Sylvius, or the foramina of Luschka and Magendie, a dilatation of the third and lateral ventricles will result from back pressure. This condition is called internal hydrocephalus. Should the obstruction occur in the basilar cisterns or in the branches of the cerebral sulci, as often happens following meningitis, a dilatation of all the ventricles is likely to occur, and this condition is designated as communicating hydrocephalus.

Figures 3 and 4 are lateral and posterior-anterior views which show the normal basilar cisterns and ventricular system

very clearly. It is a rather interesting fact that none of the sulci were filled in this case, although we had no reason to believe that the baby had ever had meningitis. The fourth ventricle is much more distinct in infants than in adults because of the absence of large mastoids and because the basilar portion of a baby's skull is not

FIG. 4. A posterior anterior view of the case shown in Figure 3.

very thick. The anterior edges of both lateral ventricles are sharply defined.

It is Dandy's opinion that normal sulci should always fill, and that the absence of such filling indicates a blocking of either the basilar cisterns or the sulci themselves. In our series of 14 cases, the sulci were well filled only four times, whereas the ventricles were filled ten times. In 4 cases there was some questionable filling of a few of the sulci. Since the ventricles appeared normal in most of the cases in which the sulci did not fill, there probably was no hydrocephalus present. We do not feel, therefore, that a failure of the sulci to fill always indicates a blocking of these structures. It is at present impossible for us to offer a reasonable explanation of this finding.

Several cases in our series were considered definitely pathological and three of them will be cited briefly.

CASE I. A male child aged three years, was brought to the hospital because of mental sluggishness and inability to talk. He had shown tardy development. The first teeth appeared at the age of two. He began to walk quite late. He had been very apathetic. He never cried nor drooled and made no attempt to talk.

At the time of the examination, the pulse was 90 and the temperature 98.8°F. The

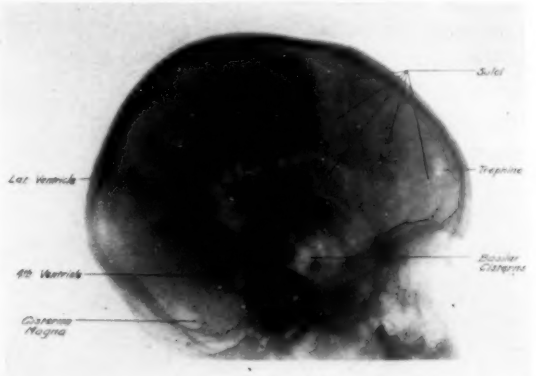


FIG. 5. A lateral view of the skull which shows the configuration of the cerebral sulci. The injection was done through lumbar puncture and not through the trephine shown in the frontal region.

FIG. 6. A lateral view of the skull of an adult made following spinal injection. The sulci are very well shown and appear to fill normally.

child showed normal development and normal weight. The features were somewhat suggestive of Mongolian idiocy. The pupils were equal and reacted well. The eye grounds were essentially negative except that the right was pale and indistinctly outlined. The brain segment areas were normal. There was a general diminution of strength. The reflexes were slightly active.

Figures 7 and 8 show posteriorlanterior and lateral views of the head. The first, second and third ventricles are clearly outlined and are moderately dilated. For some reason the fourth ventricle cannot be made out. An irregularly shaped passage is made out in the region of the chiasmatic cistern, but no sulci can be detected. It seems possible that there may be a blocking present in the basilar cisterns; possibly as a result of meningitis. The diagnosis of hydrocephalus is certainly justified on the basis of the findings and it must of necessity be the communicating type since the lateral ventricles were filled by spinal injection.

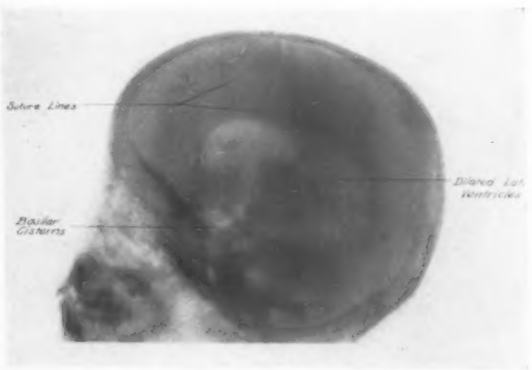


FIG. 7. A lateral view of the skull of a patient having a communicating hydrocephalus.

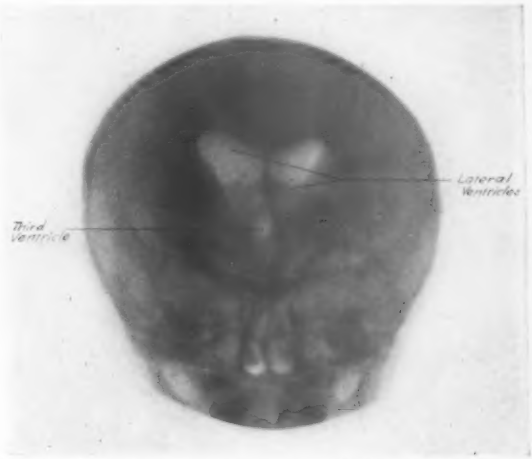


FIG. 8. A posterior anterior view of the skull shown in Figure 7.

CASE II. A male patient aged thirty-one came to the hospital because of paralysis of both legs.

He had always been subject to sore throats. About six weeks before the onset of his present illness he stepped on a nail and developed an abscess at the point of injury followed by abscess formation, tenosynovitis and lymphangitis.

His present illness began with a sudden severe pain in the left hip-joint six months ago. There was a rapid loss of the use of the left leg. By midnight both legs were completely paralyzed and he developed loss of sphincter control, intense headache and a fever of 103°F. The loss of sphincter control lasted thirty-six days and was followed by precipitate action. Following the subsidence of the acute symptoms, he noticed a dulling of both touch and pain sensation over both legs, most marked on the right. He also had intense headaches at intervals.

On examination he was found to have a temperature of 98°F. a pulse of 72 and a blood pressure of 148/80. His muscular development was normal except for a hypotonic and atrophic condition of both legs. His pupils were widely dilated but contracted readily to light and accommodation. The brain segment areas were normal. There was anesthesia to touch and temperature over the right leg as far up as the level of the trochanter. The pain sense was dull over the same area except for a strip along the lateral and posterior borders of the thigh in the upper two thirds. The medial portions of both buttocks showed insensibility to touch, pain and temperature. Over the left leg, heat and temperature sensibility were lost up as high as the level of the trochanter and there was an impairment of touch sensibility as high as the crest of the ileum. The deep reflexes and the cremasterics could not be elicited. Slight adduction of the left thigh could be accomplished and feeble movements at the left knee joint could be brought out. There was a complete paralysis of the right leg. The Wassermann was negative for both the blood and the spinal fluid.

A lateral view of the head, made following injection is shown in Figure 9. There is a moderate dilatation of the lateral ventricles made out and a slight filling of a few of the

sulci can be observed. Much of the detail is obscured by the thickness of the base of the skull. The headaches were, in all probability, due to the hydrocephalus, which was the communicating type and probably appeared as a result of meningitis, which caused an occlusion of a large number of the sulci. The paralysis was due to a spinal cord condition; probably a meningomyelitis.

CASE III. A female child aged nine, was brought in complaining of headaches, blindness, one-sided deafness and paralysis. She had an enlarged head at birth, but appeared at that time to be healthy and normally developed. At the age of three she developed sick headaches and vomiting attacks. At about the same time she stopped using her right hand and began to limp. Two years ago deviation of the eyes to the right and dimness of vision appeared. Five months later she became deaf on the left side. During the past year she has been unable to walk and has become totally blind.

At the time of examination, her temperature was 99° F. and her pulse 72. The head was enlarged and showed special prominence of the parietal bosses. The occipitofrontal circumference measured 59.0 cm. The eyes were held in conjugate deviation to the right with nystagmus. The pupils were widely dilated, the left being larger than the right. Both pupils reacted sluggishly to light. The eye grounds showed extreme pallor of both discs with an obscuring of the outlines. Voluntary movements of the eyes were limited in all directions. There was slight facial weakness on the right side and total deafness on the left. There was spastic paresis of all extremities; more marked on the right. The deep reflexes were hyperactive. No abdominal reflex was obtained on the right. Ankle-clonus and the Babinski were obtained on both sides. Gordon and Oppenheim reflexes were elicited. There was generalized weakness of the right arm and the movements of the lower extremities were not coordinated. The muscle sense and touch, pain and temperature sensibility appeared to be normal. The Wassermann was reported negative for both the blood and the spinal fluid.

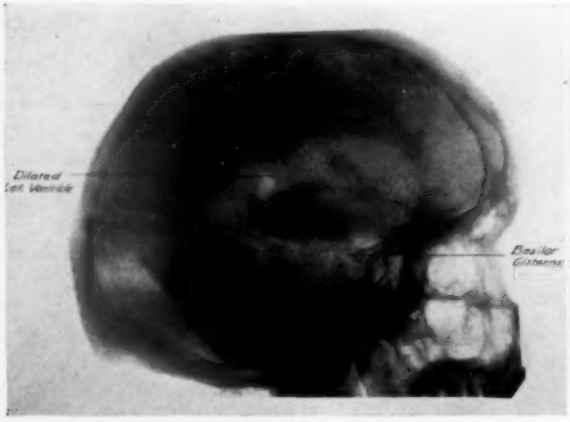


FIG. 9. A lateral view of the skull of an adult suffering from communicating hydrocephalus.

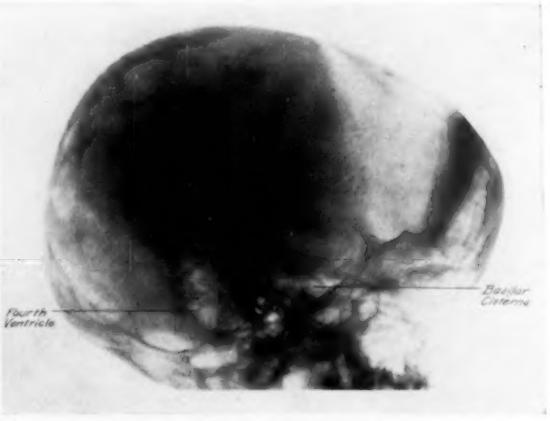


FIG. 10. A lateral view of the skull of a patient suffering from an internal hydrocephalus probably caused by a midbrain tumor.

A lateral view of the head, made following injection is shown in Figure 10. The skull is definitely enlarged and shows in the posterior parietal region, the convolutional atrophy which is usually a result of long-continued intracranial pressure. The cisterna magna, the fourth ventricle and the basilar cisterns are filled with air. The remaining ventricles and the sulci are not filled. This suggests an obstruction in the aqueduct of Sylvius. The fourth ventricle appears unusually large, and we are at a loss to explain this finding. It has occurred to us that in such cases the filling of the sulci is prevented by the increased intracranial pressure. In order to diagnose this

case more definitely a ventricular puncture should be done through a trephine so that the lateral ventricles might be studied. They should show a marked dilatation. A clinical diagnosis of midbrain tumor probably arising in the quadrigeminal bodies was made.

SUMMARY

Injection of the subarachnoid space with air appears to be a relatively safe procedure where the cases are properly selected. The after-effects of the injection are not serious. The proper interpretation of roentgenograms of the skull made following such injections should aid materially in improving the mortality statistics now credited to brain surgery.

BIBLIOGRAPHY

1. Bailey, Percival. *Arch. Neurol. and Psychiat.*, April, 1921.
2. Ransohoff, J. *Tr. Sect. Surg. and Anat. Am. M. Assn.*, 1902, p. 426.
3. Heuer, G. J., and Dandy, W. E. A report of seventy cases of brain tumor. *Johns Hopkins Hosp. Bull.*, 1916, xxvii, 224–237.
4. Bruns. Some observations on the growth and survival-period of intracranial tumors, based on the records of 500 cases, with special reference to the pathology of the gliomata. *Proceedings of 17th Inter. Med. Congress*, London, 1913, Section 7, Part 1, 203.
5. Tooth, H. H. Some observations on the growth and survival-period of intracranial tumors, based on the records of 500 cases, with special reference to the pathology of the gliomata. *Proceedings of 17th Inter. Med. Congress*, London, 1913, Section 7, Part 1, 203.
6. Krause, Fedor. Chirurgie des Gehirns und Rückenmarks, 1911, p. 572.
7. Cushing, Harvey. *J. Am. M. Assn.*, January, 1915, lxiv.
8. Dandy, W. E. Ventriculography following the injection of air into the cerebral ventricles. Am. J. Roentgenol., Jan., 1919, vi, 26. *Ann. Surg.*, Oct., 1919, lxx, 397. *Surg., Gyn. and Obst.*, April, 1920, xxx, 329. *Surg., Gyn. and Obst.*, Oct., 1920, xxxi, 340. *Johns Hopkins Hosp. Bull.*, Mar., 1921, xxxii, 67.

TUBERCULAR EPIPHYSITIS OF THE GREATER TROCHANTER*

BY D. Y. KEITH, M.D.

LOUISVILLE, KENTUCKY

THE case reported in this paper aroused interest when we began to search the literature for a description of this particular lesion. Only two of six recent textbooks of orthopedic surgery, used in our search, mentioned this type of infection, and then only very briefly. One showed a poor reproduction of the condition with no description of it.

In Peabody's report† he states that the index of all diagnoses made in the wards in the Massachusetts General Hospital since 1870 showed tuberculosis of the greater trochanter occurring only 5 times. During the past ten years the diagnosis of bone or joint tuberculosis had been made 3,062 times, and in that period only 3 times did the diagnosis of tuberculosis of the greater trochanter appear. None of these was operated on in the early stage, all developing abscesses and breaking down spontaneously; secondary infection, sinuses, recurring abscesses, etc., following.

The case reported by Peabody is the only one found in the medical literature at our command, and he states that in the current medical literature for the past ten years he has found no case reported.

Case Report. Male, aged twelve. No history of tuberculosis in the family or associates.

Personal History. Boy has had the diseases of childhood. No other serious illness. Has no local adenopathy. At age of two years drank a small quantity of kerosene and was said to have shown sugar in his urine for a period of nearly two years subsequently. (Mother's statement.)

Present History. In November, 1920, during a rest period at a football game, his feet were forcibly knocked from under him by a larger boy. This caused him to

* Read at the Midwinter Meeting of the Central Section of The American Roentgen Ray Society, Chicago, Ill., February 22, 1922.
† *Boston M. and S. J.*, June, 1921.

fall, striking directly on the greater trochanter of the right femur. He suffered considerable pain and it was with difficulty he was able to walk to his home. He did not complain during the following few days, though he says he felt quite sore; and his mother insists that for several weeks following the accident he had a decided limp. For several weeks he was under the care of a physician, and on January 13, 1921, he was *x*-rayed by Drs. Hickey and Evans. The report follows.

"Plate made of the pelvis shows normal appearance of the head of the femur. The right trochanter in its epiphyseal development shows marked irregularity and quite a change from the normal appearance, as indicated by the trochanter of the left side. We think there has been a localized injury here which has resulted in irregular bone proliferation. There is also a slight change in the angle of the neck. We see no change, however, in the epiphyseal line of the head of the femur, which we would expect if this were to be regarded as a case of adolescent rickets. Plate was made of the femur which shows no evidence of injury to the shaft."

FIG. 1. Examination April 7, 1921. Note the bony irregularity on the diaphysis. Note the irregularity and destruction of the epiphysis for the greater trochanter. Note the infiltration in the soft structure above the epiphysis.

Patient was first seen by us on April 7, 1921. He was a well-developed boy of the washed-out blond type, presenting a tumor over the right hip posteriorly and laterally, with enlargement of the superficial veins. Motion in all directions was restricted and painful.

On aspiration of the tumor by the surgeon, a few drops of turbid fluid were obtained, which, on microscopic examination, revealed no information.

Roentgen-ray examination of the pelvis showed the left hip and trochanter normal. The epiphysis for the trochanter on the right side showed a definite area of bone destruction on the superior and external aspects, extending down to the external portion of the adjacent diaphysis. There were bone proliferation and islands of bone in the surrounding soft structures, definitely separated from the diaphysis of the femur and the epiphysis of the greater trochanter. The bone destruction from the epiphyseal line of the trochanter extended on the diaphysis for approximately 1 cm., ending in a spur of elevated bone 1 cm. in height. There was no change in the acetabelum or head of the femur. The epiphyseal line for the head of the femur was normal.

FIG. 2. Examination Jan. 13, 1922. Note the smooth contour of the epiphysis of the greater trochanter as well as the area on the diaphysis, and the lessened density of the soft structures.

In the soft structures above the right trochanteric epiphysis there is a shadow

the size and shape of a normal kidney (2½ by 5 inches), which is much more dense than the surrounding soft structures, though more radiable than the normal bone; this shadow is probably a thickening of the dense fascia lata from infection.

Roentgen Ray Diagnosis. 1. Neoplasm, destructive sarcomata. 2. Osteomyelitis, probably tuberculous.

Operation by Dr. B. F. Zimmerman on April 22, 1921. The mass was incised and the macroscopic appearance was that of a degenerated tumor. There was a thin turbid

FIG. 3. Photomicrograph of greater trochanter of the epiphysis showing typical tubercles. (Signed) Stuart Graves, pathologist.

fluid in the fascial planes, which was removed, and a piece of the tissue was excised for microscopical study. The wound was left open for the purpose of radium application, should it prove malignant. The tumor mass was disturbed as little as possible.

Clinical and Surgical Diagnosis. Degenerated sarcomata.

Microscopical examination by Drs. Stewart Graves and J. D. Allen showed a number of tubercles in almost all the sections.

Diagnosis. Tuberculosis.

On April 29, 1921, the boy was again subjected to operation. The incision was enlarged and all the fungoid material removed. The bone was curetted and the wound packed with iodoform gauze. The recovery was entirely satisfactory, the wound healing completely in three months' time, there being very little discharge at any period. The pathologist's report follows.

"Gross description: Specimen consists of several bits of pinkish gray, soft tissue, the largest 20 × 8 mm. Microscopical diagnosis: 1. Tuberculosis. 2. No evidence of neoplasm."

Roentgen-ray examination on Aug. 16, 1921, showed a definite spur on the diaphysis of the right femur near the trochanteric epiphyseal line. The epiphysis of the right greater trochanter was quite irregular, though of the same density throughout. There was very little infiltration of the soft structures.

Patient was last seen January 13, 1922, and presented over the greater trochanter a thick though flexible scar, 5½ inches in length and 2½ inches in breadth, with a decided depression over the upper portion of the greater trochanter. There was a tendency to keloid formation in the scar.

Roentgen-ray examination (January 13, 1922) showed that the irregular bone which has been described was smooth both on the femoral diaphysis and the epiphysis of the trochanter. There are, however, a few islands of bone in the soft structures but with very little infiltration.

CONCLUSION

The clinical history, physical and roentgen-ray examinations pointed toward a neoplasm. There was a definite history of trauma, followed by a limp, and formation of a tumor in the soft structures with marked enlargement of the superficial blood supply. The definite hypertrophy of superficial blood-vessels is quite characteristic of sarcomata. The amount of bone destruction without bone production seen upon the roentgenogram, according to Baetjer, would correspond to a bone tuberculosis, as he definitely states that there is never any new bone produced in a

tuberculous bone infection unless a mixed infection is introduced after operation with a resulting sinus tract.*

With the amount of destruction of bone of the trochanteric epiphysis with extension on to the diaphysis, and increase in density of the adjacent soft structures with a definite tumor shadow, which we now know was the wall of the abscess cavity, a diagnosis of infection should have been positive.

The epiphysis of the greater trochanter is not different from the epiphyses in other locations and is probably more frequently infected with tuberculous bacilli than has been reported in the literature. Bone infection is certainly more frequent than new growth.

In this case bony changes were noted by roentgen-ray examination sixty days after injury, though no diagnosis was made by roentgenologists of unquestioned ability and very wide experience.†

If we have from our original plates, lantern slides and reproductions given information contributing to better diagnoses by roentgenologists, our purpose in presenting this paper will have been accomplished.

DISCUSSION

Dr. Hickey. The presentation of this case is certainly very interesting and I think Dr. Keith is to be complimented on the way he has worked it out. At the time we saw the patient his appearance was such that we did not think he had a sarcoma, and we did not feel like making a diagnosis from the plate. The patient disappeared from our observation and we were very glad to hear from Dr. Keith regarding him. I must confess that I still have a lurking suspicion that it might be sarcoma. I would like to know whether any cultural inoculations in animals were made with pieces of tissue or whether the tissue was stained for tubercle bacilli. Between a pathologist and a clinical surgeon of good experience I think I would take my choice with the diagnosis that the surgeon makes against the microscopic diagnosis. My reason is that often the diagnosis based on microscopic tissue is made from very small pieces which are not always characteristic of the entire lesion, whereas the surgeon has a chance to see the lesion in its entirety.

Dr. Lewald. My mind seems to run along the same lines as Dr. Hickey's. I would like to have absolute proof that the tuberculous nature was established beyond doubt. We did the same thing in our first case of syphilis of the stomach. The pathologist reported that it was tuberculous. We immediately asked for a revision of his study and whether he could demonstrate tubercle bacilli. He went so far as to state that he could not prove that this was a tuberculosis, and he was willing to admit that the opinion of the surgeon was correct—that this case was syphilis of the stomach. As time went on, it was proved beyond doubt that it was. I think if one wants absolute proof of tuberculosis, inoculation of animals with the tissues should be made.

We had a case in which an extraneous shadow proved to be a bursitis of the trochanteric bursa. That case was clinically diagnosed as probably a sarcoma involving the trochanter. It was the bursa overlapping the trochanter, and at operation it was found that the trochanter was filled with broken-down material; but there was every indication that it was a bursitis. That was an older patient, an adult case. I think Dr. Keith's case is of great interest.

Dr. Evans. I believe the figures are misleading and that there are more of these cases. I cannot give the figures available but I am sure that we have seen more than a dozen cases of infection of the greater trochanter, not only infected with tuberculosis but with acute infections. I believe the primary lesion is a bursitis and the general involvement is secondary to the involvement of the bursa. I believe it is very common and that this is a rather favorable location for the infection.

Dr. Keith (closing discussion). I want to thank the gentlemen for the discussion. My mind runs very much like Dr. LeWald's and Dr. Hickey's—I was sure this was a sarcoma and I stated this in the report. That was the clinical diagnosis and also the operative diagnosis, but the tissue was submitted to two pathologists, one of whom is known to be very accurate as far as technique is concerned, who will not express himself unless he is very positive. He reported on both examinations that it was tuberculosis. The other man said that the mere fact that there were tubercles present was evidence that it was an old healed area, but that there was no absolute proof that it was not malignant.

As for inoculations in animals, I am sure there were none made. It was not in the report. The fluid obtained on aspiration showed nothing on cultures; it was absolutely sterile. As to whether there were any cultures made at the time of operation, I do not know.

In Peabody's report he mentioned several

* Baetjer, F. H. and Waters, C. A. Injuries and Diseases of the Bones and Joints. New York, 1921.

† Note. June 15th, 1922. To date the patient remains well, which we believe should verify materially the diagnosis of a tubercular epiphysitis instead of sarcoma.

cases of bursitis which he had seen. He reports two cases, one of sarcoma and one of tuberculosis, in both of which they missed the diagnosis. The cases were operated on at the same time and were in the wards together.

Whether the figures are misleading, I cannot say, as we are simply reporting the figures in the literature. I think it is a very difficult thing to tell whether we were dealing with sarcoma or infection.

THE EFFECT OF RADIUM ON THE NORMAL TISSUES OF THE BRAIN AND SPINAL CORD OF DOGS, AND ITS THERAPEUTIC APPLICATION*

BY EUGENE P. PENDERGRASS, M.D., J. M. HAYMAN, JR., K. M. HOUSER AND V. C. RAMBO

Departments of Roentgenology and Surgical Research

University of Pennsylvania

PHILADELPHIA, PENNSYLVANIA

THE discovery of the selective action of radium upon tumor cells together with the daily crying need for tumor therapy has created a somewhat unusual condition in modern medicine. A large amount of interest centers around the action which radiation has upon malignant cells, and some of the most detailed studies have been made by investigators in this connection. This, however, is but one aspect of the effect of the rays upon the living cell, and we believe that an increased knowledge of the reactions exhibited by normal tissues is necessary before the real nature of the processes set up by radiation can be revealed. To treat properly any malignant tumor, one must know, if possible, the effect of radium upon the normal as well as the malignant cells. There has been comparatively little work done to show the effect of radiation on the brain; then, too, there is some discrepancy in the dosage due to the impure salt used, and the doses given have been so small that they would be of little value in therapeutic application.

Such a situation makes it necessary to discover and emphasize not only the possibilities, but also the limitations and the dangers which are inherent in a substance which possesses the powers for good or evil that are characteristic of radium.

In this paper we wish, therefore, to present the results of an experimental study of the effects of radium radiations upon the normal tissues of the brain and spinal cord of dogs, both by surface application and implantation. This work was begun with the purpose of determining the safe limit of dosage for work on these tissues in the human being, but certain findings have made it advisable to consider the subject from a broader standpoint, and to bring together and weigh the results of the work, which can be found in the literature. We will consider the clinical symptoms, gross effects, and microscopical pictures produced by various doses applied to the brain and spinal cord. For our present purposes the microscopical study must of necessity be limited to the practical consideration of the matter of the distance to which the rays penetrate, as shown in the sections. A more intensive study of the extremely interesting sections must be reserved until time and opportunity permit a study which shall give a comparison of our findings with known lesions of the brain and cord. We will have to consider the general effects of radium, the manifest toxemia, and finally, certain findings which may throw some light on the nature of the general effects which we have observed.

Danysz[1] was the first worker to study the effects of radium upon the tissues of the central nervous system. He placed a tube containing one centigram of a "very

*A Leonard Prize Paper

active" radium salt over the spine and part of the skull of a mouse one month old, the tube being placed beneath the skin. The mouse developed paralysis and ataxia in three hours, convulsions in seven hours, and died in eighteen hours. Mice one year old treated the same way did not die for six to ten days. Three guinea pigs, eight to twelve days old, which had had the same tube beneath the skin over the lumbar cord for twenty-four to forty-eight hours, developed a complete paralysis of the posterior part of the body in one to three days, and died with convulsions a few days later. Adult guinea-pigs and rabbits, similarly treated, showed no nervous lesions. They succumbed some weeks after operation, probably as the result of infection due to the destruction of the skin. An adult rabbit which had had the tube on its dura for eight hours, a trephine opening having been made, showed no symptoms for two days, but developed a hemiplegia on the third day.

In a later paper[2] Danysz records the results of exposing mice, confined in small wooden cages to 23 and 50 mgm. of radium bromide, which was fastened in a hole in the lid of the cage. The duration of exposure varied from four hours to twenty days. The reactions consisted in alopecia, dermatitis, paralysis and death, the latter occurring in from ten to forty-four days, depending on the age of the animal and the length of exposure. Microscopic examination showed, especially, vascular disturbances, broken capillaries and the nervous substance "swimming" in the blood. No changes were found in the nerve cells.

Schotz,[3] after fastening 25 mgm. of a radium salt on the heads of rabbits for one to three hours, found a peculiar intense injection of the meninges. He found similar changes in mice, exposed in small chambers, but no gross areas of softening. No microscopic report is given.

London[4] exposed young mice in a small glass cage to 30 mgm. of radium bromide fastened upon the cover. They all died in four to five days. The first symptoms were reddening of the ears, blinking, sleepiness, and weakness, followed by paralysis, coma and death. The reflexes were increased during the coma. At post morten he found hemorrhages into the subcutaneous tissue and dura, and the greatest microscopical changes in the skin and cerebral cortex. In another paper[5] he reports the finding of atrophic nerve cells in the cords of three rabbits exposed for a long time to a small amount of radium.

Heineke[6] found deep hemorrhagic areas of softening, spreading from the site of application in a rabbit which had carried 20 mgm. of radium bromide on its head for fourteen days, the dosage being 6,720 mgm. hours. The rabbit was well until the third week, when it died with general spastic symptoms.

Obersteiner,[7] working with mice, found that a diffuse radiation of the head produced large and small hemorrhages into the cerebrum, cerebellum, and medulla, with some round cell infiltration around the vessels. The nerve cells were for the most part unaltered, some of the anterior horn cells in the cord, however, showing changes in the granules. He notes that while the severity of the symptoms depends on the age of the animal, the duration of exposure, and the amount of radium used, there seems also to be a variable factor of resistance in different individuals. The different symptoms after exposure are, for the most part, directly or indirectly, the expression of the circulatory and metabolic changes produced by the radium, and the impressive symptoms referable to the nervous system are accounted for by the fact that this system responds most easily to the influences mentioned.

Alquier and Faure-Beulien[8] found only minute hemorrhages, without discoverable change in the nerve elements, after therapeutic applications of radium, applied externally to the heads and cords of rabbits. There was no disturbance of the general health.

In the above experiments, except those of Danysz, the radium was placed either on the scalp or some distance above in the roof of the cages, and radiation was with unfiltered rays.

Horsley and Finzi[9] placed 55 mgm. of radium bromide on the pre- and post-central gyri of monkeys for two and a half to four hours. The rays were filtered through 0.5 mm. of platinum and 1 mm.

of rubber. No animals showed any symptoms up to the time they were killed, after twenty-six to forty-five days. Examination of the brains showed thickening of the dura with an infiltration of the pia and arachnoid by erythrocytes and leucocytes. There was an endothelial proliferation in the blood-vessel walls, in some places, even occluding the lumen. There were punctate hemorrhages in the first two layers of the cortex. No changes in the nerve-cells were found, except where hemorrhage had taken place.

In comparison with this, the results of Wago[10] obtained by exposing the surface of the brain of rabbits to the radiations from a Krommayer mercury quartz lamp, are interesting. He found chromotalysis, kariolysis, karyorrhexis and other changes in the nerve-cells, most intense in the superficial layers of the cortex. He could not recognize any change in the neuro-fibrils even when the cells were well degenerated. Young rabbits were much less resistant than full-grown ones.

Williamson, Brown and Butler[11] reported the effect of doses of 200 to 900 mgm. hours on the normal brain tissue of the dog, the tubes being placed beneath the dura on the surface of the brain. None of the dogs showed any clinical symptoms up to the time they were killed three weeks after operation. Two dogs which were not killed showed no symptoms up to seven weeks. At autopsy the surface of the brain showed an area of hyperemia down the center of which was a black necrotic strip. Microscopically the great majority of the cells in this area were completely destroyed, the blood-vessel walls were three or four times their normal thickness, hyalinized, and congested, but their walls were intact. Marking the area of necrosis was a circle of hemorrhage, where the vessels were not thickened, but had ruptured. Beyond this area the vessels were congested but their walls and the nerve-cells in this region appeared normal.

Halkin,[12] after exposing small areas of the skin to a small amount of radium salt for one to two hours, could discover no histological change after twenty-four hours. The first change, seen on the third day, was a widening of the capillaries, followed in a few days by a slight perivascular infiltration, followed by swelling and vacuolization of the endothelial cells. Still later, the capillaries had become broad blood spaces, with small hemorrhages around them. This was regarded as a paralysis rather than an inflammation, for the infiltration was slight. This early and pronounced effect of radium on the small blood vessels has been noticed by many later observers, and is often looked upon as a primary and perhaps essential effect, upon which all other findings are to be based.

We have applied doses of 1,000–2,600 mgm. hours well-filtered radium to the brain cortex, doses of 450–1,000 mgm. hours unfiltered radium implanted into the brain substance, by means of radium needles, and doses of 300–1,200 mgm. hours well-filtered radium applied to the dorsal cord. For all operations the dogs were under surgical anesthesia with ether. The side of the head was shaved and painted with iodine. An incision was made from above and behind the eye to above and in front of the ear, extending down to the temporal muscle. The muscle was cut downward and forward, in the direction of its fibers, retracted laterally, and a trephine opening 1 cm. in diameter made in the skull. This was enlarged with rongeur forceps, as was necessary to accommodate the radium tube, or to allow the insertion of the needles. On account of the size of the tube and needles used, it was necessary to make the opening over the parietal lobe. Radiation of the motor area alone, which might have given results of some interest, was impracticable on account of the size of the tube, the shape of the dog's skull, and the forward position of the motor area in the dog's brain. When a tube was used, the dura was not opened, the tube being placed on the dura. The dura is not thick enough to have any appreciable effect on the rays, and the removal of the radium was greatly facilitated, and the danger of mechanical injury to the brain lessened, by this method. In the first operation when the tube was inserted beneath the dura the mechanical injury gave rise to a hernia cerebrae, and consequently this method was abandoned. The muscle was sutured, and the subcutaneous

tissue and skin sutured separately. A silk thread was attached to the tube, (or needle), brought out through the muscle and subcutaneous tissue, and folded under the skin, which was sutured over it. When the radium was to be removed, this silk thread was caught on a blunt dissector, and the tube gently drawn out. Another stitch was then put in the subcutaneous tissue where the thread had been, and the skin wound closed. Attempts were made to protect the muscle from the rays by placing a small piece of lead over the tube, but so much difficulty was experienced in removing it, that it was not done routinely. The tubes used for the surface application measured 2–2.8 cm. long, .3–.5 cm. in diameter, and were .4–.5 mm. thick. They were made of platinum or silver.

With the exception of one dog (22) all dogs receiving a dose of 1,150 mgm. hours or below gave no symptoms until necropsy was performed. Dog 22 was a dog which had been operated on before, a gastro-enterostomy having been done with a low loop of bowel. At autopsy no gross lesion could be found in the brain. To what degree death was due to the previous operation, or whether the radium had a much more severe effect upon this dog in his weakened condition than it would have had on a normal dog, is problematical.

All dogs, except one, receiving a dose of 1,400 mgm. hours or above, died. The exception (dog 20, Table I) is supposed to have received a dose of 2,500 mgm. hours, which should have caused death in about fourteen days. There is a possibility that the dog only received 1,250 mgm. hours, due to the fact that the radium might not have been placed in one of the silver capsules inserted into the cranial cavity. Another possibility of error is that the radium capsule might have slipped out of the cranial cavity into the muscle flap. This seems improbable, however, as there was no necrosis of the muscle flap. The only other explanation we have is the possibility that we may be dealing with an increased individual resistance in this particular dog.

The gross lesions of the brain found at autopsy varied greatly, the variation depending upon the time that had elapsed

TABLE I
EXPERIMENTS ON SURFACE APPLICATION

Dog No.	Dose in Mgm. Hrs.	History	Result
29	360	No symptoms for 2 months. For a while seemed blind and showed peculiar circus movements. Seemed to recover.	Killed after 10 months
30	900	No symptoms for 2 months. Occasional convulsions during the summer, but none for 4 months before death.	Killed after 9 months.
22	500	Gradually grew weaker after operation. See below.	Died in 7 days.
28	542.5	.....	.....
19	1,000	No symptoms.	Killed the 14th day.
17	1,150	No symptoms for 7 weeks.	Killed the 49th day.
1	1,400	No symptoms for 3 weeks. Then restlessness, followed by gradually increasing weakness.	Died 28th day.
9	1,800	.....	Died 17th day.
5	2,100	No symptoms for 1 week. Then vomited some. Developed weakness of the hind legs during 2d week. Superficial infection in skin incision.	Died 14th day.
27	2,200	No symptoms for 1 week. Eighth day sick, gradually grew weaker. Fourteenth day lay quietly on side, could not be aroused. No localizing symptoms. Killed. Viscera negative.	Killed 14th day.
16	2,300	Well 1 week. Eighth day slight weakness right side. Eleventh day very weak. Unable to stand. Lay helplessly on side; could not be aroused.	Killed 11th day.
14	2,400	Well 1 week. Ninth day languid and a little weak. Tenth morning very sick; could not be aroused. Died about noon.	Died 10th day.
20	2,500	No symptoms for 4 weeks.	Killed 29th day.
18	2,600	Well 4 days. Weak and sick on the 5th.	Died 6th day.

since the radium application. Thus a dog which died one week after receiving a dose of 500 mgm. hours showed no gross lesion, as mentioned above. Dogs with doses of 2,300–2,600 mgm. hours and living eleven days or less presented a dark reddish-brown, apparently sharply circumscribed, oval area on the surface of the brain, studded with bright red dots. This area averaged 20 × 10 mm., and extended inward 10 mm. from the surface of the brain at its deepest point. In two dogs with smaller doses, 1,800 and 2,100 mgm. hours, which lived slightly longer, seventeen and fifteen days respectively, the color of this apparently sharply circumscribed area had changed to a dull grey, and was surrounded by a darker grey halo. On cross section, the area still appeared sharply circumscribed. In these dogs there was no disturbance of the contour of the brain surface. A dog killed on the forty-ninth day, after having survived a dose of 1,150 mgm. hours, and showing no clinical symptoms, presented a similar area, but of a decided yellow color, measuring 15 × 23 mm. In the center of this area was an excavation, with irregular jagged base and margins, 12 × 16 × 3 mm. Cross section showed that the necrotic area extended into the brain 12 mm. from the surface. Beyond this area were small punctate hemorrhages as far as the internal capsule. These small punctate hemorrhages were also seen in a dog dying twenty-eight days after a dose of 1,400 mgm. hours.

A dog killed ten months after an exposure to 360 mgm. hours of radium, and showing the clinical symptoms mentioned above, presented at autopsy a healed scar on the surface of the brain in the parieto temporal region. This area was greyish in color and slightly depressed. The area measured 15 × 8 mm. Cross section showed a dark brown, irregular area extending 8 mm. beneath the cortex. While the outline of this area was irregular, its margin appeared very sharp and distinct from the grossly normal brain tissue beyond.

Another dog which was killed nine months after an exposure to 900 mgm. hours showed at autopsy a large, fairly well defined, irregular, crater-like excavation on the left parieto temporal region. The edges of the crater were rough and jagged, with shreds of necrotic tissue hanging from them. This crater measured 20 × 10 mm. Lying loose in this cavity at autopsy was a shrunken laminated blood clot, covered on the outside with yellow hemosiderin pigment. On cross section the blackened homorrhagic and necrotic area extended into the brain substance 10 mm. from the edge of the crater, which was 15 mm. deep at its deepest point. Grossly this area of necrosis and hemorrhage, while irregular, was sharply circumscribed.

One of the questions of vital importance is the extent of the effect of the radium. This problem might be approached in two ways, both of which methods we have followed to a certain extent.

The first method would be to expose the brain to small doses of radium, and then compare the area of destruction of the brain after the animal had lived a long period of time with the lesions produced by similar doses at earlier stages. The purpose of such a procedure would be to determine whether the area involved is greater in dogs living for a long period than appears in dogs living a shorter time. From this standpoint, the extent of the destruction in the dogs allowed to live a year is found to be considerably greater than that seen after three weeks. From this finding it is evident that the effect of radium is more insidious and far-reaching than could be concluded from short-time experiments, and its full effect can only be seen after a long time.

The second method of study of this particular problem is by the application of refined histological methods. This is manifestly a special part of the work, and will require a comparison with known pathological conditions of the nerve cells, and therefore a detailed description of these results does not belong in a general discussion of the problem.

At the present time we are amply justified in stating that far-reaching effects upon the cells are demonstrable in sections. These findings fully explain the gross lesions seen in the long-time experiments just described; definite conclusions as to the nature of these cell changes can

only be reached by comparison with recognized changes in nerve-cells due to causes other than radiation, a study manifestly exceeding the scope of this paper.

The sections show distinct evidence of involvement of the various tissues of the brain, at least as far again as the areas of necrosis and hemorrhage seen grossly. The salient changes are endothelial proliferation of the intima of the blood-vessels, perivascular infiltration, and degenerations of the nerve-cells and fibers.

In this connection it is interesting to bear in mind the work of Hertwig,[13] who found that radiated spermatozoa still possessed their general cellular function of penetrating the ovum, thus starting the process of fertilization, but had lost their specific nuclear function whereby the nucleus of the spermatazoon takes an equal part with the nucleus of the ovum in development. From the standpoint of the nuclei the egg developed parthenogenically. In other words, the radium has exerted an effect upon the nucleus of the spermatozoa, too delicate to affect the function of the cell as a whole, but which could be clearly demonstrated by loss of specific nuclear function. Therefore, in judging the effect of radiation, the possibility of delicate nuclear changes far beyond extent of gross lesion and even beyond the extent of histological demonstration should be borne in mind.

The radium needles used for implantation measured 2.8 cm. long and 1.5 mm. wide, and contained 10 and 12½ mgm. of radium. They were made of thin non-corrosive steel, which, being very thin, does not act as a good filter; thus allowing the penetration of a large percentage of beta rays. The needles were sterilized in 10 per cent formalin solution for fifteen minutes and in 95 per cent alcohol for forty-five minutes. Two needles were used in each dog. A small opening was made in the dura, over the parietal lobe, one needle inserted in a forward direction, toward the motor area, keeping it nearly parallel with the surface of the brain, at a depth of about 7 mm., in order to avoid striking the internal nuclei: the other implanted vertically in a similar maner, running toward the temporal lobe.

The first striking result of these implantation experiments compared with surface application is the much more rapid development of a general toxic condition, as shown by dogs 23 and 24. The development of a general peritonitis in two of the others, without local signs of infection, would point to a general lowering of resistance by the radium, and even the fifth dog, in spite of the meningitis, showed a generalized infection not usually associated with post-operative meningitis.

TABLE II
IMPLANTATION EXPERIMENTS

Dog No.	Dose in Mgm. Hrs.	History	Result
23	360	No symptoms for 2 days. Then began to be sick, general weakness, especially in the hind legs. Sixth day very sick, could hardly be roused, rapid difficult breathing. No local or general infection.	Killed 6th day.
2	450	No symptoms for 5 days, then restless, and gradually increasing weakness. Post mortem, meningitis, pleuritis, peritonitis, pericarditis, multiple abscesses in liver, hemorrhagic pancreatitis.	Died 7th day.
8	450	No symptoms for 5 days. Very weak by eighth day. Eleventh day general clonic convulsions. Post mortem peritonitis, viscera negative except congested kidneys.	Killed 11th day.
4	900	Dog sick and languid all the time. Post mortem, generalized peritonitis, viscera negative.	Died 5th day.
25	Control	Glass rods size and shape of needles used. No symptoms up to 17 days. Post mortem, viscera showed nothing abnormal.	Killed 17th day.

It seems almost unnecessary to point to the fact here that radium is not very effective on bacteria, and that therefore radium needles must be carefully sterilized and inserted under the most strict asceptic precautions. But even then, we believe, the strange results we have here recorded can only be explained on the hypothesis of

the lowering of the resistance of the entire body to invading micro-organisms.

More intense reactions would naturally be expected from implantation of the radium into the brain substance than from the surface application of an equivalent dose, as, in the former instance, the brain is receiving the entire radiation, whereas in the latter, approximately half of the radiation is lost. However, the results from implantation seem to point to an effect not observed at all with surface application. This, we feel, is due to the fact that in the implantation experiments, radium needles were used. The thin steel surrounding the radium was a poor filter and the brain substance received a large quantity of beta ray radiation. This in addition to the gamma ray radiation, caused the intense reaction, and subsequent toxemia.

In the application of radium to the spinal cord, an incision was made over the spinous processes corresponding with the segments of the cord noted below; the muscle masses were separated on either side from the lamina. Three spinous processes were cut off with bone forceps and the lamina removed with rongeur forceps until there was sufficient room to place the radium tube on the dura over the cord. The wound was closed by the same method as that used in the head operations, and the same method of removing the tube was employed.

TABLE III
EXPERIMENTS ON SURFACE APPLICATION TO THE SPINAL CORD

Dog No.	Dose in Mgm. Hrs.	History	Result
13	300	No clinical symptoms.	Killed 48th day.
11	600	Developed weakness in the hind legs followed by spasticity in 6 weeks. This went on to a spastic paralysis in the 7th week. Complete paraplegia. Moderate spasticity of thigh muscles, virtually none in lower leg. Flexion and crossed extension, reflexes feeble. Scratch and stepping reflex and extensor thrust could not be elicited. Patellar reflex brisk.	Killed in 10th week.
10	900	Eighth thoracic segment. Marked spasticity of hind legs in 2 weeks. Spastic paraplegia in 3d week.	Killed end 4th week.
12	1,200	Twelfth thoracic segment. Spastic paralysis of hind legs before end 2d week.	Killed end 2d week.

In none of these dogs was there any involvement of the sphincters. There was no paralysis of the forelegs. Attempts to test for loss of sensation were unsatisfactory.

Grossly a slight discoloration at the level of the lesion in dogs 10 and 12 was all that could be seen. Histologically dogs 11, 10 and 12 showed tract degeneration and various degrees of changes in the nerve-cells for two segments above and below the lesion. Dog 13 showed an appreciable amount of tract degeneration and abnormal nerve cells at the level of the lesion. The fact that marked clinical symptoms are produced by an exposure of 600 mgm. hours, a dose which produces only a very insignificant gross lesion, indicates the probability of extensive and serious physiological changes in the brain far beyond the extent of the gross lesion. This is borne out in the histological sections. Hence great caution must be used in estimating the effect of a dose of radium by the size of the gross lesion produced.

The local tissue destruction is by no means the only effect of the application of radium to the surface of the brain.

There is a considerable increase in the weight of the radiated hemisphere, ranging from 12.6 to 42.8 per cent. This fact was stumbled on by accident when a number of experiments had already been completed; so that the list of weighed brains does not include the entire series.

The weights of the two hemispheres of 9 normal dogs which had been obtained after pharmacological experiments showed an average difference in weight of 0.63 per cent, and a maximum difference of 1.8 per cent (Table IV). This small difference in the two hemispheres of the brain is rather striking when the normal variations in the weights of the other paired organs of the body are considered. A similar correspondence in the weights of the two hemispheres in sheep has been found by Donaldson.[14]

He found an average difference of 1 per cent in a series of 53 cases.

The weights of 6 treated brains are seen in the accompanying table (Table V). The brain of dog 22 which died one week after operation, showed a difference of only 1.1 per cent, which is within the normal limits.

It will be noticed that the increase in weight of the treated hemisphere seems to bear more relation to the time the dog lived after operation than it does to the doses of radium. Thus dogs 16 and 19 with doses of 1,000 and 2,300 mgm. hours respectively, showed practically the same increase of weight. On the other hand, dog 20, which received a dose of 2,500 mgm. hours, but lived until killed on the twenty-ninth day, showed the greatest increase. In this brain the difference was easily appreciable to the eye. The whole hemisphere looked bigger, the convolutions were flattened, the sulci less prominent, and on section the tracts of white matter appeared much broader in the treated than in the untreated hemisphere.

An attempt was made to determine, if possible, whether this increase of weight in the radiated hemisphere was due to edema. The brain of a dog killed two weeks after an exposure to 1,000 mgm. hours of radium was carefully removed, separated from the cerebellum, and the brain stem divided just above the corpora quadrigemina. The forebrain was then cut into three pieces by a transverse cut, and then into six parts by a longitudinal cut. Each piece was then placed in a separate glass desiccating jar and weighed. They were then frozen by placing the jars in the refrigerating apparatus used for storing cadavers, for twenty-four hours. Next the jars were put into a desiccating oven and dried in vacuo at a temperature of 48°C. to constant weight. From these weights the total wet and dry weights of each hemisphere were calculated. A second brain, that of the dog which survived the dose of 2,500 mgm. hours, was treated in a similar way, except that the temperature of the oven was increased to 98°C. The weights of these two brains are seen in Table VI.

TABLE IV
WEIGHTS OF NORMAL BRAINS

Dog No.	Left Hemisphere, Gm.	Right Hemisphere, Gm.	Left Heavier, Gm.	Per Cent	Right Heavier, Gm.	Per Cent
1	30.84	30.96	0.12	0.3	....	...
2	22.35	22.28	0.07	0.3	....	...
3	40.51	40.69	....	...	0.18	0.4
4	29.99	30.21	....	...	0.22	0.7
5	22.95	23.01	....	...	0.06	0.2
6	33.78	33.26	0.52	1.6	....	...
7	27.78	27.81	....	...	0.03	0.1
8	29.94	30.49	....	...	0.55	1.8
9	32.75	32.85	....	...	0.10	0.3

Average difference 0.63 per cent. Maximum difference 1.8 per cent.

TABLE V
WEIGHTS OF TREATED BRAINS

Dog No.	Dose in Mgm. Hrs.	Treated Hemisphere, Gm.	Untreated Hemisphere, Gm.	Difference, Gm.	Per Cent Increase
22	500	30.44	30.10	0.34	1.1
19	1,000	36.28	31.11	5.17	16.5
27	2,200	38.85	30.42	8.43	27.7
16	2,300	35.45	30.45	5.00	16.4
20	2,400	39.08	27.35	11.72	42.8
18	2,600	36.40	32.30	4.10	12.6

TABLE VI
TOTAL SOLIDS IN RADIATED AND NORMAL HEMISPHERES

	Radiated Hemisphere	*Unradiated Hemisphere*	
Dog 19. Dose 1,000 mgm. hrs.			
Wet weight	36.26	31.11	
Dry weight	7.15	6.86	
Per cent solids	19.7	22.0	
Per cent water	80.3	78.0	
Radiated side heavier..	Wet weight, per cent....		16.5
	Dry weight, per cent....		4.3
Dog 20. Dose 2,500 mgm hrs.			
Wet weight	39.08	27.35	
Dry weight	6.24	5.42	
Per cent solids	15.9	19.8	
Per cent water	84.1	80.2	
Radiated side heavier..	Wet weight, per cent....		48.2
	Dry weight, per cent....		15.1

The increase in the dry weights of the radiated hemispheres, and the consequent rather close agreement of the percentages of solids and water in the two hemispheres is rather difficult to explain. There would seem to be three possibilities; first, that there had been a cellular increase in the radiated hemisphere, due to the action of the radium. The second possibility is that the radium has given rise, directly

or indirectly, to a process of hydrolysis, so that some of the water is held in chemical combination and is not lost by desiccation at the temperature used. The third possibility is that the increase in dry weight is due to the solid matter derived from lymphatic fluid which had previously occupied the hemispheres giving rise to an edematous condition of the treated side.

The first proposition is responsible for this increase in dry weight only in a very small degree, if at all, because histological study shows no such extensive cellular infiltration or proliferation.

In attempting to prove or disprove the second idea, the total nitrogen of the treated and untreated hemispheres of dog 27 was determined by the method of Stehle.[15] The increase of the total nitrogen on the treated side is sufficient to disprove the second theory.

This difference, however, is not inconsistent with the third view, but, on the other hand, rather supports it. For if we assume that the difference in weight of the two hemispheres, 8.43 gms., is due to edema—distention of the lymph spaces and flooding of the tissues with a lymph-like fluid—we can come to the following conclusion: We know that lymph contains approximately 5 per cent protein,[65] therefore in an increase of 8.43 gm., 0.4215 gm. must have been due to protein substances. This would contain 0.067 gm. nitrogen, since 6.25 gm. protein contain 1 gm. of nitrogen. The difference in the two analysed hemispheres was 0.075 gm. of nitrogen. The discrepancy of 0.008 gm. is within the limit of error of the experiment.

Hence we are inclined to assume that the observed increase in the weight of the treated hemisphere can be accounted for entirely by an existing edema.

We have already noted the fact that an exposure of greater than 1,400 mgm. hours was followed by death, with a single exception (dog 20). With this single exception the animals have responded so uniformly that the results follow, when plotted with doses in mgm. hours as abscissae, and length of life after operation as ordinates,

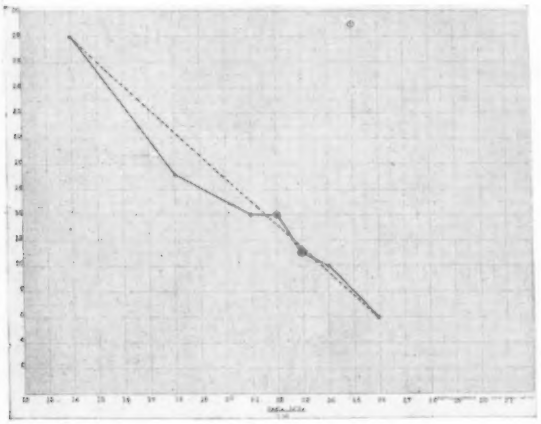


FIG. 1. $\frac{\text{mgm. hrs.}}{100}$

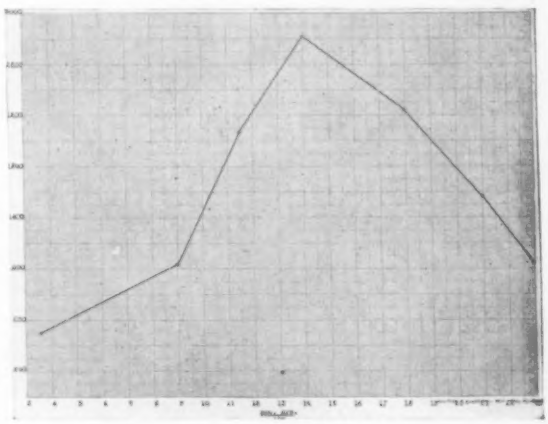


FIG. 2. $\frac{\text{mgm. hrs.}}{100}$

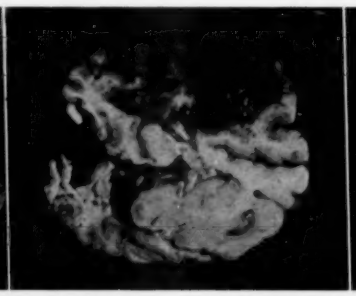
almost a straight line (Fig. 1). In fact, following this graph, it was possible to predict within one or two days the time of death of an animal. This result shows very clearly that the cause of death must be sought in some other factor than the loss of function of the destroyed area.

In the first place the animals did not show symptoms of loss of cerebral function. They were apparently in the best of health, with no localizing signs, as paralysis. The only symptom noted at all was a possible weakness in the hind legs. Then possibly twenty-four or forty-eight hours before the calculated time of death the animals became very ill with general weakness and prostration, but with still no paralysis, and died apparently from increasing weakness. Symptoms derived from the gastrointes-

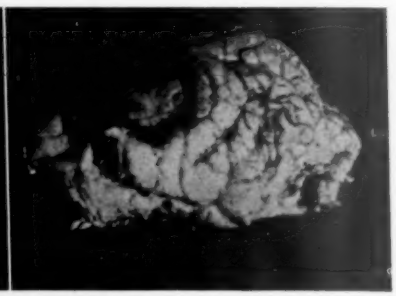
tinal tract were not in evidence, a point to be borne in mind in the later discussion of roentgen-ray toxemia.

A second reason for considering that the fatal result is not due to the loss of function of the injured brain is found in Figure 2, in which the total volume of destruction seen grossly, calculated as half an ellipsoid of revolution by the formula corded on the cord, and also from the gross findings in the brains of the two animals that had lived for almost a year after small doses. In these two animals the size of the lesions was far in excess of that seen in the animals autopsied a short time after equivalent doses. Nevertheless the two factors taken together indicate clearly that the cause of death is not due to local effect,

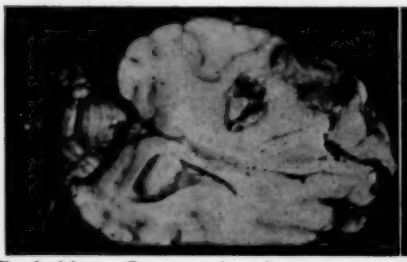
Brain No. 1. Received 1400 mgm. hrs. surface application.



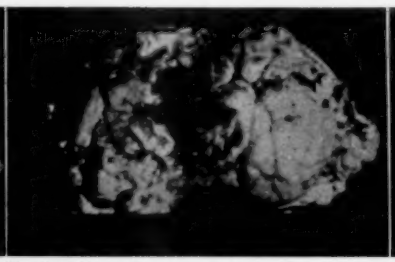
Brain No. 1. Cross section shows extensive destruction of brain tissue. Dog lived twenty-eight days.



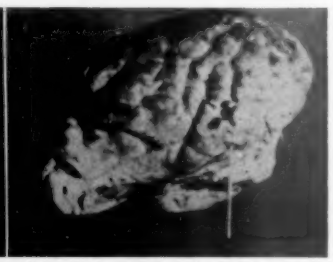
Brain No. 4. Received 900 mgm. hrs. implanted into brain substance.



Brain No. 4. Cross section shows comparatively little destruction of brain tissue. Dog died fifth day.



Brain No. 5. Received 2100 mgm. hrs. (surface application) also had infection of wound. Photograph shows extensive necrosis. Dog died fourteenth day.



Brain No. 9. Received 1800 mgm. hrs. surface application. Photograph shows that there was very little destruction of brain tissue. Dog died in seventeen days.

$V = \int_0^a y^2 dx$, where x and y are given by the equation of the ellipse $\frac{x^2}{a^2} + \frac{y^2}{b^2} = 1$, are plotted as ordinates, and the dose in mgm. hours as abscissae. It is seen that the total volume of gross destruction, in spite of increasing dosage, falls rapidly after the dose has reached a size which results, as seen in graph Figure 1, in the death of the dog at an earlier time. It might be argued that the gross area of destruction is no criterion of the total effect of the radium; and this is no doubt true, as shown in our microscopic studies of the brain and from the experiments just re-

but to some general condition of toxemia.

The existence of a toxemia after exposure to either *x*-rays or radium was early recognized both by clinicians and experimental workers, and considerable literature has been produced in the discussion of the possible source of this toxemia. The results of different observers have been somewhat at variance, and different theories have from time to time controlled the opinions of investigators. In order to show these fluctuations in opinion, we will review the more important papers in chronological order, rather than attempt to group them with respect to the principal point stressed.

Walsch,[16] in 1897, reported that an *x*-ray

demonstrator, who had been under his care, suffered from headaches and dizziness for two months, after he had been exposed to the *x*-rays for some time.

Schwarz,[17] in 1903, advanced the first definite theory of the modus operandi of the radium radiations. After placing 20 mgm. of radium on the shells of hens' eggs for one hundred and forty-four hours, he found only insignificant changes in the shell and albumen, while that part of the yolk exposed to the full effect of the radium was of a greenish color, stiff, and could easily be lifted out from the rest of the yolk. It had the strong unpleasant taste of spoiled cod liver oil. He believed that these changes were determined chiefly by a decomposition of lecithin, in which embryonal cells are particularly rich.

The same year, Bohn[18] came to the conclusion that radium acts chiefly on the chromatin of the nucleus, augmenting its activity or destroying it, according to the duration of the exposure.

The next year, in discussing the action of radium on the tissues, Schaper[19] took his stand with Schwarz.

Neuberg,[20] however, did not agree with Schwarz. He explains the effect of radiation as due to the destruction of all the cellular ferments except the autolytic ones, so that in tumor tissue after exposure there is (*a*) a loss of the vital ferments, and (*b*) an increased activity of the autolytic ferments.

Heile,[21] on the other hand, finding an increased metabolic rate after exposure to *x*-rays, and particularly an increase in the excretion of uric acid and the purines, was inclined to assume that by these rays one can produce an increase in the autolytic processes in the living body, and in such fashion that not only the cells of the tissues themselves are destroyed, but that the leukocytes which have wandered in and later gone to pieces, give an increased amount of enzymes. He compares the process to the autolysis of dead organs in the absence of bacteria, resulting in products similar to those of tryptic digestion, and quotes the work of Hoppe-Seyler and others to support this view. The increased excretion of the purines he accounts for by the autolysis of the nucleo-proteins.

Brain No. 8. Received 450 mgm. hrs. implanted into brain substance.

Brain No. 8. Cross section shows the destruction of tissue. Dog was killed eleventh day.

Brain No. 18. Received 2600 mgm. hrs. (surface application). There is some necrosis of brain tissue and the area of hemorrhage surrounding necrosis can be seen.

Brain No. 30. Received 900 mgm. hrs. Photograph shows extensive destruction of tissue.

Brain No. 30. Cross section shows extensive destruction of brain tissue. Dog killed after living nine months.

Henri and Mayer[22] note that beta rays of radium will precipitate positive colloids, but are without effect on the negative colloids. The oxyhemoglobin of the dog and frog was changed to methemoglobin and slowly precipitated, while carbon-monoxyhemoglobin was unchanged. The red blood-cells were rendered less resistant to hypertonic salt and sugar solutions by exposure to radium. They compare their results with those of Schwarz, and conclude that the action of the radium is on the lecithin, which is known to be one of the constituents of red blood-cells.

Darier[23] claimed that low intensity radium radiations over the peripheral nerves produced an analgesic effect.

Baermann and Linsen[24] maintained that the chief effect of the *x*-rays was on blood-vessels. Thies[25] repeated Schwarz's experiments, but could detect no change when he exposed lecithin itself to radiations. He claims that change in the lecithin cannot be responsible for the tissue changes, and thinks it more likely that the primary effect is on some cell substance which plays a rôle in the cell division, giving rise to the irregular division seen in radiated cells.

Lange,[26] writing in 1905 on the constitutional symptoms seen clinically after *x*-ray treatment, concluded that the reaction was due to an acidosis produced by the breaking down of the cells under the treatment.

Edsall[27] at this time noted an increased excretion of urea, uric acid, and the purine bases, and a general stimulation of metabolism after *x*-ray and radium treatment, and believed this due to stimulation of autolysis. In another paper[28] he found the greatest destruction in the bone marrow, spleen, and lymphoid tissue, and concluded that the destruction was most marked in the tissues rich in nucleoproteins.

Linser and Helber[29] and Rosenstern[30] claimed that long exposure to the *x*-rays produced nephritis. Buschke and Schmidt,[31] and Krause and Ziegler,[32] on the other hand, held that any renal changes were slight and transitory.

In 1906, Bouchard and Balliazard,[33] in a most interesting paper, reported the distribution of radium emanation in the different tissues of the body after placing radioactive barium sulphate contained in collodion sacs in the peritoneal cavity of guinea-pigs. They measured the amount of emanation by estimating the electrical conductivity communicated to the gases extracted from the organs by a mercury pump, the increased conductivity of the gases being due to the presence of the emanation. One gm. of suprarenal tissue contained 4.7 times as much emanation as 1 gm. of spleen; 11.4 times as much as an equal amount of lung tissue; and 15, 60, and 100 times as much as skin, liver, and kidney tissue respectively. This is interesting when the relatively considerable percentage of lecithin and neurine in the suprarenal capsule is considered.

Work on enzymes of various kinds was being pushed by various writers: thus Wilcox[34] stated that exposure to radium was without effect on tyrosinase, Lowenthal and Edelstein[35] that the autolysis of tissues in vitro was accelerated by the presence of radium emanations in the water added to the tissue, while Richter and Gerhartz[36] claimed that *x*-rays were without effect on enzymes and that the results recorded by other workers were due to experimental errors. It remained for Richards to coordinate these results.

Werner, in a number of papers,[37–43] reported his observations on the effect of radiation on lipoids, and on the effect of injection of lecithin and cholin. He found that lipoids are made more labile and favorable to autolysis by radiation. By subcutaneous injection of lecithin he duplicated the effect of radiation on the skin. Cholin injections produce the same effect on the white blood cells as does *x*-ray exposure, and also the same degeneration of the epithelium of the testicle. Injections of cholin in human beings produced diarrhea, vomiting, sweats and pain.

Opitz and Meyer,[44] in 1906, noted a rise in blood pressure, followed by slowing of the heart and a fall in blood pressure after intravenous injection of radium bromide in dogs.

Berg and Welker[45] found that exposure to radium was without material effect on protein metabolism.

Edsall and Pemberton[46] maintained that

the toxic reaction seen in leukemia after *x*-ray treatment was due to the sudden demand on the organism for the complete disintegration and excretion of the many products of tissue breakdown. With an inability to accomplish this, there is a halting of the normal metabolism, and intoxication results.

Working on the theory that roentgen rays act as a ferment accelerator, thus speeding up metabolism, these workers record some success in treating unresolved pneumonia by roentgen rays.

Warthin[47] found that roentgen radiation over the kidney region produced swelling of the epithelium of the renal tubules, with changes in the chromatin and some loss of the staining powers of the cells. The cells recovered shortly, secondly developing cloudy swelling.

Engel[48] reported a study of the constitutional effects following roentgen-ray treatment. He noted nausea, vomiting, pain, followed by depression and accompanied at times by palpitation or tachycardia.

By exposure of pregnant bitches to *x*-rays, with the abdomen protected by a lead plate, Hippel and Pagenstecher[49] produced either cataracts in the eyes of the young, or abortion, or death of the embryo, the latter in about the same frequency as after direct exposure of the abdomen. Choline injections gave identical results, without giving rise to any symptoms in the mother.

Werner and Lichtenberg[50] found that injections of choline would interrupt pregnancy in rabbits, and they also call attention to the close imitation of roentgen-ray effects that can be produced in a chemical way.

Regaud, Nogier, and Lacassagne,[51] 1912, after some experiments on dogs in which exposure to roentgen rays led to abortion, anorrhexia, diarrhea, cachexia, and in some instances death, conclude that the roentgen rays exercise a powerful cytolytic effect on the stomach and gastrointestinal tract, with remarkable atrophy of the glands, especially those of Lieberkuhn, if the animal lives long enough.

Packard[52] suggests that radium radiations act indirectly on the chromatin and protoplasm of the cell by activating the autolytic enzymes which bring about a degeneration of the complex proteids and probably affect the other protoplasmic substances in the same manner.

Richards,[53–56] in a number of papers, 1914–1917, on the effect of exposure of enzymes to *x*-rays and radium, showed that a short exposure accelerated the enzyme action, while longer exposure inhibited, or destroyed it altogether. Between these there was a point where exposure was without effect. He suggests that the effect of radiation on the enzymes is due to hydrolysis of the zymogen; hence its more complete transference into active enzyme. With longer exposures the dissociation of the electrolyte may be supposed to occur in amounts sufficient to precipitate the colloid enzyme particles, and thus remove them from solution. When these two processes balance, radiation is non-effective.

Pfahler,[57] in a paper in 1916, discussing the cause of the nausea, vomiting, and prostration seen after roentgen-ray treatment, says they are probably due in great part to the gases generated in the neighborhood of the high tension currents, and to hypersensitiveness on the part of the patient.

Millet and Miller[58] reported in 1918 the post-mortem examination of a patient who had been treated for cancer with large doses of radium. No trace of the carcinoma could be found, nor any morbid process that could explain death. No blood studies were made. They conclude that in addition to the local action of radium there is "evidence of a more general effect whose nature we do not at all understand."

Luden[59] found that exposure to radium reduces the cholesterol content of the blood, and reduces the high cholesterol values commonly found in carcinoma.

Hall and Whipple,[60] in an excellent discussion of the toxemia following *x*-ray exposure, call attention to the similarity of the effects that can be produced in dogs by proteose injection, and regard both as true non-specific intoxications, associated with much destruction of body protein. If there is any renal trouble, it is slight and not constant. They conclude that after a lethal dose of *x*-rays to dogs there is a

latent period of twenty-four hours or more followed by vomiting and diarrhea until death, which is generally on the fourth day. A greater dose does not change the clinical picture. The non-protein nitrogen of the blood is greatly increased the day before death, the urinary nitrogen is increased on the day after exposure and remains high until death. Post mortem they found mottling of the intestinal mucosa and destruction of the epithelium. They think the injury to these cells may account for the intoxication associated with the vomiting and diarrhea.

Denis and Mortin,[61] from their work on rabbits, believe that constitutional symptoms of intoxication follow exposure to the *x*-rays only when some part of the intestinal tract is radiated.

Gudernatsch and Bagg[62] by subcutaneous and intravenous injection of radium emanation in pregnant rats produced death of the embryo with areas of hemorrhage in the subcutaneous connective tissue and along the meningeal vessels. They conclude that the effect of radium on endothelium may be selective.

That the effects of radium are insidious, and that its power is little understood and not fully appreciated is evidenced by the recent report,[63] of three deaths from aplastic anemia at the London Radium Institute, in spite of the great care used for the protection of the workers. This is particularly significant, coming as it did only four weeks after the report of the death of Dr. William I. Bruce from the same condition.[64]

It is evident from the review of the literature that many minds have engaged themselves with a study of the problems of the general toxemia following radiation by *x*-ray and radium. The theories offered may be divided into three groups.

The oldest theory, and one which from some points of view still remains attractive, is that advanced by Schwarz.[17] This theory would explain the specific effect of radiation upon the young cells and other cells rich in lecithin by the production of choline from the breakdown of the lecithin. This theory has been severely attacked by numerous writers, but two facts nevertheless remain, in spite of the criticism; first, choline injections can reproduce certain of the so-called specific effects of radiation, namely, the destructive effect upon spermatogenesia, the causation of foetal cataracts, and even the sensitization of the skin to the *x*-ray; secondly, injections of choline can apparently reproduce the general symptoms noted by Hall and Whipple in their study of *x*-ray toxemia.

The second theory looks for the explanation in the effect upon the chromatin of the nuclei of the cells. This theory finds convincing support in the work of Hertwig who found the striking effect upon spermatozoa referred to above, namely, the loss of nuclear activity in a cell which still retains its cellular functions.

The third theory seeks the explanation in the increased autolytic activity of the radiated tissue, or, as some would express it, the inhibition of the other processes of cell death. This theory would explain the general symptoms of toxemia on the same basis as the theory now accepted for the cause of death in high obstruction of the intestinal tract (Whipple) or acute pancreatitis (Sweet,[66]) in both of which conditions the cause of the general toxemia is found in the activity of the proteolytic ferments of the body; since these ferments are in all cells, an autolysis of any tissue might set free the same series of toxic processes.

Now we must note that the symptoms which characterize our observations are not at all like those noted by Hall and Whipple in *x*-ray toxemia. The symptoms which they observed pointed to an involvement of the gastrointestinal tract, while in our animals these symptoms were not present. Furthermore, it should be noted that the clinical symptoms of a general nature seen after the use of radium in the uterus, for example, point to a primary effect on the gastrointestinal tract.

These three theories are reducible to two, and the apparent discrepancy between the toxemia seen in our work and that described as *x*-ray toxemia, as well as the toxic symptoms seen clinically after using radium in the uterus, can be cleared away. First we have an effect upon the nucleus, perhaps the primary and essential effect,

as we might conclude from the work of Hertwig. The histological study of our sections, a study which will be reported later, shows an effect upon the cells far beyond the zone of vascular and gross injury. After the death of the nucleus, or coincident therewith, the cell dies, and the tissue becomes subject to autolysis. The direction of this autolysis will depend upon the predominating material of which the cell is composed. It is stated that "those cells which are most actively engaged in the synthesis of a given compound seem to be equipped with more of the necessary enzyme than are other cells less actively engaged in this particular type of metabolism." (Bradley [67]).

The only change in the original theory of Schultz is that the breakdown of the lecithin in living tissue is not due to the direct, chemical action of the radiation, but to a stimulation of the lipase found in connection with cells rich in lipoids; the first and the third theory are one and the same.

The stimulation of autolysis, or the creation of conditions favoring autolysis, as a result of the radiation, produces a picture dominated by the type of substrate chiefly present in the tissue; most of the tissues, being largely composed of protein, would show the influence of the proteolytic ferments, with a resultant picture of intoxication due to the products of proteolysis, as seen in the work of Hall and Whipple, and in the clinical picture after using radium in the uterus.

In our work, however, the lipase of the brain (Pagenstecher,[68]) breaks down the lecithin-lipoid compounds which are present in the brain in larger amounts than in other tissues, with the setting free of choline and neurine. Neurine may be set free directly, since some authors claim that it is found in brain tissue; it is also formed chemically by the simple dehydration of choline, in fact, the literature on choline and neurine is much confused, because of the close chemical relationship of the two substances. Neurine exercises an effect upon the voluntary muscles similar to curare[69] which would explain the symptoms of marked asthenia exhibited in our experiments.

We offer as a working hypothesis of the action of radiation upon living tissue that it is due to a primary effect upon the nucleus and the resultant death of the cell under conditions favoring autolysis. The direction of the autolysis will depend upon the predominating material of which the tissue is composed; and we will have as a result a toxemia in the one case due to proteolysis, in the case of the experiments here reported, a toxemia due to the products of lipolysis.

CONCLUSIONS

1. An exposure of the normal brain tissue up to 1,150 mgm. hours is compatible with life (surface application).

2. The results on the cord, however, would indicate that exposure of vital areas of the brain as well as exposure of the cord should never be made by surface application or implantation.

3. Microscopic studies indicate that considerable changes are to be found with exposures that give no clinical symptoms.

4. The brain after exposure of 1,000 mgm. hours shows a general swelling throughout the entire radiated hemisphere, which, from our studies, must be ascribed to the production of an edema which is not limited to the radiated area, but extends throughout the entire hemisphere.

5. Radiation of the brain by radium (surface application and implantation) can produce severe general symptoms which indicate that a powerful toxin has been produced from the radiated tissue.

6. The effect of radium is due to a two-fold action; first, an effect upon the nucleus and cytoplasm of the cell, which causes, secondly, the death of the cell under conditions favoring autolysis. The direction of this autolysis is determined by the chief component of the radiated cells. If this be protein the toxic products of proteolysis may exhibit their general effect. If the chief component be lipoid compounds, we believe that the resultant autolysis may free the toxic components of lecithin, and produce their characteristic reactions.

7. The use of radium as a therapeutic agent in the treatment of brain tumors is recommended, but should be undertaken

only after one is thoroughly familiar with the dangers that may come from improper use thereof.

8. We believe our experiments on the dogs are applicable to human beings, because it is not the destruction of brain tissue that causes death, but some toxemia, and in the application of radium in the treatment of malignant tumors of the brain of humans the normal brain tissue should not receive more than 1,150 mgm. hours.

THERAPEUTIC APPLICATIONS

Malignant tumors[70] of the brain are somewhat different from malignant tumors found elsewhere, in several characteristics: they are usually very slow in growth; the cardinal symptoms, such as visual disturbances, headache, nausea and vomiting usually appear late; they usually do not metastasize. Very often the tumors are unlocalizable, even after exploratory craniotomy, and, finally, they are sometimes inoperable.

Thus one can see that there is a field for some physical agency such as radium, which will not only arrest the growth of a malignant lesion, but even lead to a process of retrogression.

In the treatment of brain tumors by radium there are a number of problems one must consider. In this paper we do not wish to go into the technique of application but only the types of brain tumor in which radiation should be employed.[71]

1. When a brain tumor is exposed after craniotomy and is considered inoperable, provided this tumor is localized and not of the infiltrative variety, direct implantation of radium into the growth is recommended. It is not safe to give dosage sufficient to destroy the entire growth, as this might entail too much exposure of normal brain tissue at a given location. To supplement the implantation, crossfire radiation by radium should be employed over as much of the scalp surrounding the tumor as is deemed necessary and of value. By this procedure the likelihood of causing considerable destruction of normal brain tissue and a possible toxemia is lessened. By clinical observations crossfire radiations of radium cause fewer general symptoms than does implantation. In the implantation of radium, one should be careful to insert it far enough below the surface of the lesion, so as to prevent a possible necrosis of the muscle flaps.

Direct implantation is only recommended in the growths easily accessible, and should the tumor be near vital centers of the brain, the dosage given should be governed by this, so as to prevent a possible loss of function of a given center. This danger is a real one, as evidenced from our spinal cord experiments wherein marked clinical symptoms were present even after small dosages.

2. In brain tumors partially removed, well-filtered radium should be packed in the center of the cavity made by the partial removal of the tumor. The dosage should depend on the amount of tumor tissue left, and as above should be supplemented by crossfire radiation through the scalp.

3. In brain tumors which are not localizable even after exploratory craniotomy, crossfire radiation by radium through the scalp should be given a thorough trial.

4. There are a number of brain tumors which infiltrate the brain substance. Crossfire radiation alone should be employed in this type of growth.

5. In the treatment of spinal-cord tumors we feel that one should not attempt to apply radium to the surface of the lesion, or implant radium into it. A large number of spinal-cord tumors give clinical manifestations early, are localizable, and can be removed surgically. In the cases where the cord tumors are removed, post-operative radiation by radium or *x*-ray is recommended.

6. Careful sterilization of all radium tubes or needles used in surface application or implantation, is very important, our method being to place the radium tubes and needles in 40 per cent formalin for thirty minutes and 95 per cent alcohol for forty-five minutes.

From our experiments we have drawn the following conclusions in regard to radiation in the treatment of brain tumors and from them a safe technique has been arrived at. Radium is recommended:

1. As a prophylactic against recurrence after removal of brain tumors.

2. As a prophylactic against recurrence after sella decompression.

3. As an active agent in the treatment of cases of recurrent visual disturbances after sella decompression has been performed.

4. As an active agent by direct implantation into inoperable tumors supplemented by crossfire radiation through the scalp (external application).

5. As an active agent in cases where brain tumors are only partially removed, by implantation of radium into the center of the cavity, and supplemented by crossfire radiation externally.

6. As an active agent by crossfire radiation (external application) in brain tumors which cannot be localized or discovered by operation.

7. Treatment of spinal-cord tumors should be restricted to crossfire radiation by the roentgen ray or radium, as in surface application there is a great possibility of causing paralysis.

BIBLIOGRAPHY

1. Danysz, J. *Compt. rend. Acad. d. Sc.*, 1903, cxxxvi, 461.
2. Danysz, J. *Ibid.*, 1903, cxxxvii, 1296.
3. Schotz. *Deutsche med. Wchnschr.*, 1904, xxx, 94.
4. London, E. S. *Berl. klin. Wchnschr.*, 1903, xl, 523.
5. London, E. S. *Ibid.*, 1905, lxii, 1336.
6. Heineke. *München. med. Wchnschr.*, 1903, xlviii, 2090.
7. Obersteiner, H. *Arb. a.d. neurol. Inst. a.d. Wien.*, 1905, xii, 86. *Wien. klin. Wchnschr.*, 1904, xvii, 1049.
8. Alquier and Faure-Beulien. *N. Iconog. de la Salpêtrière*, 1909, xxii, 109.
9. Horsley and Finzi. *B. M. J.*, 1911, ii, 898.
10. Wago. *Arch. Int. Med.*, 1917, xix, 801.
11. Williamson, Brown, and Butler. *Surg., Gynec.,*
12. Halkin, H. *Arch. f. Dermat. u. Syph.*, 1903, lxv, 201. *and Obst.*, 1920, xxxi, 239.
13. Hertwig, O. *Arch. f. mikr. Anat.*, 1911, lxxvii, 197, 165, 301. *Ibid.*, 1912, lxxix, 201.
14. Donaldson, private communication.
15. Stehle. *J. Biol. Chem.*, 1920, xlv, 223.
16. Walsch. *B. M. J.*, 1897, ii, 372.
17. Schwarz. *Arch. f. physiol.*, 1903, c, 532.
18. Bohn, G. *Compt. rend. Acad. d. Sc.*, 1903, cxxxvi, 1085.
19. Schaper, A. *Anat. Anz.*, 1904, xxv, 298, 314, 326, 337.
20. Neuberg, C. *Ztschr. f. Krebsforch.*, 1904.
21. Heile. *Ztschr. f. klin. Med.*, 1904, lv, 508.
22. Henri, V. and Mayer, A. *Compt. rend. Acad. d. Sci.*, 1904, cxxxviii, 521.
23. Darier, A. *Lancet*, 1904, i, 652.
24. Baermann, G., and Linsen, P. *Munchen. med. Wchnschr.*, 1904, li, 996.
25. Thies. *Mitt. a.d. Grenzgeb. d. Med. u. Chir.*, 1904, xiv, 694.
26. Lange. *J. Am. M. Assn.*, 1905, p. 65.
27. Edsall. *Tr. Ass. Am. Physicians*, 1905, xx, 279.
28. Edsall, D. L. *J. Am. M. Ass.*, 1906, xlvii, 1425.
29. Linser, P., and Helber, E. *Deutsches Arch. f. klin. Med.*, 1905, lxxxiii, 479.
30. Rosenstern, I. *München med. Wchnschr.*, 1906, liii, 1063.
31. Buschke, A. and Schmidt, H. E. *Deutsche med. Wchnschr.*, 1903, xxxi, 495.
32. Krause, P. and Ziegler, K. *Fortschr. a.d. Geb. d. Röntgenstrahlen*, 1906, x, 126.
33. Bouchard, C. and Balliazard, V. *Compt. rend. Acad. d. Sc.*, 1906, cxliii, 198.
34. Wilcox. *J. Physiol.*, 1906, p. 34.
35. Lowenthal and Edelstein. *Zeitschr. f. Biochem.* 1908, xiv, 484.
36. Richter, P. F. and Gerhartz, H. *Berl. kl u. Wchnschr.*, 1908, xlv, 646.
37. Werner, R. *Zentralbl. f. Chir.*, 1904, xxxi, 1233.
38. Werner, R. *München med. Wchnschr.*, 1905, lii, 691.
39. Werner, R. *Deutsche med. Wchnschr.*, 1905, xxxi, 61.
40. Werner, R. *Brun's Beiträge*, 1906, lii, 51.
41. Werner, R. *Med. Klin.*, 1912, viii, 1160.
42. Werner, R. *Berliner medizinischer Gesellschaft*, 1912, vii, 14.
43. Werner, R. and St. Szécsi, S. *Ztschr. f. Chemotherp.*, 1912, i, 357.
44. Opitz and Meyer. *Science*, 1906, xxiii, 332.
45. Berg, W. N. and Welker, W. H. *Science*, 1906, xxiii, 323.
46. Edsall, D. L. and Pemberton, R. *Am. J. M. Sc.*, 1907, cxxxiii 286, 426.
47. Warthin. *Am. J. M. Sc.*, 1907, cxxxiii, 736.
48. Engel, K. *Deutsche med. Wchnschr.*, 1907, xxxiii, 22.
49. Hippel, E. and Pagenstecher, H. *München med. Wchnschr.*, 1907, liv, 452.
50. Werner, R. and Lichtenberg, A. *Deutsche med. Wchnschr.*, 1906, xxxii, 1583.
51. Regaud, Nogier, T., and Lacassagne. *Arch. d'électric. med.*, 1912, xxi, 321.
52. Packard. *J. Exp. Zoöl.*, 1914, xvi, 85.
53. Richards, A. *Am. J. Physiol.*, 1914, xxxiv, 224.
54. Richards. *Science*, 1915, xlii, 287.
55. Richards, A. Am. J. Roentgenol., 1917, iv, 564.
56. Richards, A. *Ibid.*, 1915, ii, 908.
57. Pfahler, G. E. Am. J. Roentgenol., 1916, iii, 310.
58. Millet and Miller. *J. Cancer Research*, 1918, iii, 127.
59. Luden. *J. Lab. and Clin. M.*, 1918, iv, 849.
60. Hall and Whipple. *Am. J. M. Sc.*, 1919, clvii, 453.
61. Denis and Mortin. *Am. J. M. Sc.*, 1920, clx, 555.
62. Gudernatsch and Bagg. *Proc. Soc. Exper. Biol. and Med.*, 1920, xvii, 183.
63. London letter, *J. Am. M. Ass.*, 1921, lxxvi, 1360.
64. Ibid., 1921, lxxvi, 1181.
65. Neuberg. Der Harn, ii, 1020.
66. Sweet. *Internat. Clin.*, 1915.
67. Bradley, H. C. *J. Biol. Chem.*, 1913, xiii, 411.
68. Pagenstecher. *Ztschr. f. Biochem.*, 1908, xviii, 285.
69. Abderhalden, E. Handbuch, 1911, iv, 835.
70. Frazier, C. H. Surg., Gynec. and Obst., Sept., 1920.
71. Pancoast, H. K. Am. J. Roentgenol., 1922, ix, 42.

ULTRAVIOLET AND X-RAY AS PHYSIOLOGIC COMPLEMENTS IN THERAPEUSIS: A NEWLY ESTABLISHED CLINICAL TREATMENT*

BY C. M. SAMPSON, M.D.

United States Public Health Service Hospital No. 61

STAPLETON, NEW YORK

INTRODUCTION

IN provinces other than the province of medicine the method of scientific advancement is preeminently that of deductive sequel.

When the method of the scientific laboratory is applied to the study of the human organism, it is sometimes observed that the physically deduced laws either do not obtain, or obtain in so modified a form contrary to expectation, that the results are no longer recognized as born from the parent observation.

A critical survey of accomplishment in medicine points strongly to the fact that medicine is not a science as compared to the ordinarily accepted concept of physical science. In truth, medicine is an ultra science whose phenomena are myriad and defiant of ordinary scientific standards. The explanation seems to lie in the exceptionally complex structure of the human organism, a structure infinitely more complicated than even the most complicated inanimate object; and added to this already intricate organization, there must be considered that inevitable something called life for which no scientific explanation has ever yet been satisfactorily adduced.

Hence progress in medicine can be expected best along the lines already set by precedent; namely, empirical observation serving as a basis for the deduction of law, rather than law serving as the basis from which to experiment for a desired result. After all, the method of medicine is statistical. Observations are first gathered, then sorted and classified into similar groups. Finally, they are given to the laboratory scientist with the view of establishing the fundamental structure underlying the empirical observations.

There is no "scientific" theory to offer in explanation of the clinical facts presented in this paper. There are some scientific precedents referred to, from time to time, which tend to show that these empirical results have somewhere a corelated precedent in medical observation.

The apparatus used is simple, the application is without difficulty, and the clinical results are instant. The basic theme is essentially borrowed from nature. The actinic rays of the sun impinging upon the peoples of a world, become necessary for the fit survival of those inhabitants. Fit survival implies natural prophylactic measures and natural curative measures. Local actinism, therefore, increases the effects on the skin at the point applied, similarly as solar actinism is manifested on the peoples of the world. It is well recognized that solar actinism was necessary for the protection of people closest exposed to the sun; and the result was that a permanently sun-burned or dark race was perpetuated. The empirical observations of this research make use of this phenomenon which has been constantly observed.

THESIS

A comparative study of *x*-ray and ultraviolet-ray dermatitis reveals several very important differences. An *x*-ray dermatitis comes on rather slowly, usually in from eight to fifteen days or longer, while the ultraviolet-ray dermatitis comes on rapidly, generally in from three to twenty-four hours. The *x*-ray dermatitis causes the hair to fall out, and, if severe enough, is followed by permanent alopecia. The ultraviolet-ray dermatitis—no matter how severe unless compression has been used and the skin destroyed—checks the falling

* MSS. submitted in Leonard Prize Competition.

out of hair, stimulates the hair follicle, causes extra rapid growth of normal hair and often causes lanugo to take an added growth, size, and in some cases, pigment. The stronger the actinic ray reaction, the more stimulating it is to hair growth, one or two good ultraviolet-ray erythemas usually being sufficient to arrest the falling out of hair even when due to heavy *x*-ray dosages. The *x*-ray dermatitis, if severe enough, is followed by atrophic changes, ulcer formation, sloughs, or telangiectases. The actinic dermatitis—no matter how intense the overexposure if compression has not been used and the burner has been kept far enough from the skin to prevent a heat burn—is followed by desquamation or blisters, if the overexposure has been great enough, and the formation of new skin normal in every respect. An *x*-ray dermatitis increases the irritability of that area to subsequent *x*-ray doses, while the inflammatory reaction following heavy actinic dosage decreases the irritability of that area to subsequent applications of the ultraviolet ray. By means of rapidly repeated erythemas from the actinic ray, an area of skin may soon be in such a condition that it will require some fifty times the original dermatitis dose of the ultraviolet to produce even the mildest grade erythema. This increased tolerance of the skin to ultraviolet rays is not confined to the action of the actinic rays alone, but includes, to a lesser degree, the *x*-rays. Whether this increased tolerance is due solely to the tanning produced, or whether the repeated inflammatory reactions produced by the actinic rays cause the skin to lose some of its irritability, or whether the blood-chemistry changes which follow the application of ultraviolet light have an antidoting or damping effect upon the cycle of tissue changes set in train by massive *x*-ray dosage, cannot be stated positively at this time. Clinical evidence would seem to show that all three factors have a part in the increased tolerance. Surfaces tanned gradually by exposure to sunlight or weak applications of the actinic rays without noticeable erythema being produced, show a slightly increased tolerance to *x*-ray dosage, but nothing like the increase caused by repeated heavy erythemas, rapidly produced, by the quartz mercury burner. This increased tolerance seems to follow whether the surface tans or not, but possibly not to so great a degree where tanning does not take place.*

Case IV, while only a basal cell type, is included to illustrate this point. This patient's skin blistered easily, but refused to tan under the most rigorous actinotherapy, yet the reaction—or rather lack of reaction—following the roentgen-ray dose was the same as in the other cases. This holds true with all other cases of the same peculiar skin that we have treated so far. One man with a skin of exactly the same type that refused to tan after repeated heavy actinic erythemas, was given 50 ma. min. with a 4 in. back-up spark, 8 in. target skin distance, 1 mm. aluminum and 1 mm. flexible leather filter at one dose, for a general cheloidal condition of numerous gas scars over one side of face and chin, with no visible reaction; 44 men were given 45 to 50 ma. min. in divided doses in a three-week period with the same factors, with no trace of erythema in any case. Most of these men tanned well. Seven of them did not tan visibly. When attempting to explain *exactly* how the ultraviolet light applications may antidote the constitutional effects of massive roentgen-ray doses, we meet with difficulty from both sides. Although both remedies have been in use for a long time, and much is known of the clinical effects of each, little has been definitely ascertained in regard to the minutiæ as to how either produces its constitutional effects. There are almost as many theories as there are research centers. Hall and Whipple,[1] in a very instructive series of experiments with the effects of massive *x*-ray dosages upon dogs, discuss the constitutional effect, and state so succinctly the difficulties of drawing conclusions, that we shall quote them.

"Lange maintains that the reaction is the result of an acidosis resulting from cellular degeneration or from increase in

* The tanning of the skin is only *one*—and in our opinion one of the least—factors, and the subsequent vigorous actinic treatment applied after the heavy *x*-ray dosage is much more important than the preliminary treatments.

catabolic cellular activity. He submits no analyses of blood or expired air to support this claim.

"Edsal and Pemberton advanced a theory which we believe to be more nearly correct. They noted that roentgen rays sometimes produced a constitutional reaction which they ascribed to an acute intoxication. They state their belief. 'The tissue destruction accomplished by the roentgen rays undoubtedly involves chiefly tissues especially rich in nucleoprotein. The decomposition products of this form of protein are especially rich in substances that are more or less toxic and difficult to metabolize and excrete.'

"This general systemic reaction which may follow the use of roentgen rays in therapeutic doses has another appeal to the investigator. This reaction must be '*non-specific*' as no group of bacteria can possibly be concerned. If any injurious substances are formed in the body, these substances must be formed from the body tissues or fluids and not from any protein substances introduced. It seems safe to assume that the body protein must be injured in some fashion, as there is a distinct increase in urinary nitrogen and in the non-protein nitrogen of the blood. In fact, the primary injury may react upon the body protein in some manner so that the tissue autolysis of the injured protoplasm may form toxic split products* which cause further injury to the body protein—a vicious circle.

"The question of ferments and roentgen-ray exposure is a most important one. When we finish the analysis of the anatomical changes caused by the roentgen rays and the review of the clinical symptoms of intoxication which may be due to the specific action of the roentgen rays on the leucocyte or the intestinal epithelium or the epidermis, we come up against the fundamental question: How do the roentgen rays injure a living cell? It is claimed by Hertwig that the chromatin is first injured and that this injury is the

FIG. 1. Case I. Showing case the day before amputation was performed, and location of metastases.

FIG. 2. Case II. Epithelioma, with general involvement of adjacent glands.

FIG. 3. Case III, (*a*). Showing primary tumor on right clavicle and metastatic areas. Also showing absence of dermatitis after a 90 ma.m. roentgen-ray dose with a 10 in. gap.

* The validity of the split protein product theory is not generally subscribed to by the majority of immunologists nor by the writer; but the theme that seroprotein changes are involved is an established concept that requires no defense.

fundamental one. But Richards has shown that the cytoplasm is also injured. Many workers are tempted to leave the morphology of the cell and venture into the field of cellular ferments, which is equally difficult, to say the least. One must be very careful in accepting *in vitro* ferment experiments on unicellular organisms or isolated ferments to explain ferment reactions in the living complex of a warm-blooded animal.

"Yet there are observations which indicate that the body ferments in the living cells are actually influenced by the roentgen rays.* A spleen removed from a rayed animal will show more rapid autolysis than a control (Heile. *Ztschr. f. Krebsf.*, 1904, ii, 171). Our experiments indicate that the same holds for the epithelium of the intestinal mucous membrane exposed to the roentgen rays. A. Richards (*Am. J. Physiol.*, 1914, xxxv, 224; *Science*, 1915, xlii, 287), who has done the best experiments upon the roentgen rays and ferments, is able to show *in vitro* that small doses of the roentgen ray accelerate and larger doses inhibit certain ferment action. He does not believe, however, that this direct action of the roentgen rays on ferments is adequate to explain all the reactions of a living cell to the roentgen ray. This conservative opinion should have much weight.

"We should not lose sight of the fact that the roentgen rays pick out certain cells with no apparent rhyme or reason. Why, for instance, is the leukocyte injured and the pancreatic cells, which surely are rich in ferment, escape entirely? Simple disturbance of cellular ferments by the roentgen rays cannot explain any such peculiar reaction as this just mentioned. There must be some initial stimulus or injury inflicted upon certain cells of the body and other body cells must be tolerant and escape this injury or stimulus. It is

FIG. 4. Case III, (*b*). Showing metastatic areas in spine and exfoliation following overdose of actinic ray.

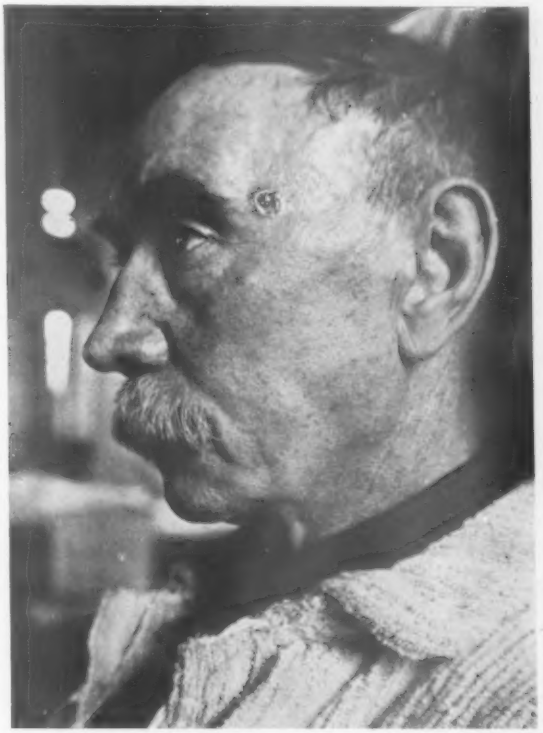


FIG. 5. Case IV. Showing type of basal cell epithaelioma, clear skin, freckled, which would not tan under actinic ray.

*Recent trend of investigation would point to the possibility of vitamine changes in *x*-ray and radium treatment. (See "Similarity of Effects Produced by Absence of Vitamins and by Exposure to *X*-Rays and Radium" by W. Cramer, A. H. Drew, and I. C. Mottram, London, D.P.H.). From the Imperial Cancer Research Fund, and from the Radium Institute, London. *Lancet*, May 7, 1921, i, No. 19, 963.

conceivable that the primary injury may form toxic split products which cause the final intoxication, but we have no right to assume this without some weight of evidence, and this experimental evidence has not been submitted.

"The word *injury* may be as good as any to indicate our belief that some change has been effected within the cell substance (nucleus or protoplasm). This change may influence, *first*, the cell protoplasm, cell lipoids, cell ferments, etc., but who is to say whether the structure or the ferment is first changed or injured by the roentgen

FIG. 6. Case V. General paronychia.

ray? We know of many fundamental changes in cells, even fatal changes, which leave no trace that can be detected by modern histological methods. Yet we cannot accept such an instance without question as an example of *primary* injury to the cell ferments. We are too apt to cloak our ignorance by the use of terms which have very little fundamental significance when subjected to analysis.

"In the face of these difficulties the authors hesitate to outline the constitutional reaction to the roentgen rays as pictured in their minds, and put forward this explanation with a proper regard for possible objections and criticisms. Exposure of a dog to the roentgen rays brings about certain changes (or 'injury') in certain of the body cells. In some cells the injury may be evident in a short time (leukocytes) and in other cells the injury may be greatly delayed (epidermis). We cannot explain this latent period. It is at least possible that other body cells may be injured after a longer or shorter latent period, depending upon the individual properties of the cells. The nitrogen elimination shows that the cell injury and autolysis begin promptly after exposure to the roentgen rays and continue with a rising curve to the fatal outcome. The blood nonprotein nitrogen speaks for the same progressive destruction of body protein. We have evidence that the ferments in certain cells of the body are profoundly altered and take part in the cell destruction beyond a doubt, yet we cannot say that this ferment disturbance is not secondary to some 'injury' of cell substance apart from the enzymes. There are individual peculiarities in the reaction of the cells to the roentgen rays which speak for an individuality in the cell reaction and this surely may not of necessity depend upon primary ferment change. The liver and pancreatic cells are rich in ferments, yet, so far as we know, they escape the roentgen-ray injury. The epithelium of the small intestine is closely related to the liver and pancreatic eipthelium, yet it appears to be 'injured' by the roentgen rays. Is this due to a primary injury of ferments? Then how may we explain the immunity of other parenchyma cells which contain similar autolytic ferments?

"The obvious 'injury' of the intestinal epithelium offers a satisfactory explanation for many of the clinical features of the fatal intoxication—vomiting, diarrhea and prostration. Disturbances of this epithelium can produce a severe intoxication (intestinal obstruction) and for this reason we think the injury of the intestinal epithelium by the roentgen rays plays no small part in the general systemic reaction and intoxication."

Subsequent experimentation by Denis, Martin and Aldrich[2] offers further proof of the correctness of some of Hall and Whipple's conclusions, but adds some very strong evidence in the behavior of the alkaline reserve curve* to the proof of the correctness of Lange's acidosis theory, which they were not inclined to favor.

In a series of studies on roentgen-ray effects by Murphy, Hussey, Wakahara and

* Lewis (unpublished communication) points out the influence of psychic influences in affecting, to a slight extent, the alkaline reserve curves in aments. These slight changes would not appear materially to invalidate the conclusions of Lewis, Martin and Aldrich.

Sturm, published in the 1921 volume of *The Journal of Experimental Medicine*, attempt is made to show the fallacy of many of the former theories, and to strengthen the lymphoid reaction hypothesis. Some of their conclusions based upon the experiments are very convincing. In Study No. vi, 301,[3] they state: "Hence it may be assumed that considerable doubt still exists that *x*-rays in a dose suitable for a living animal, i.e., an amount which will not produce a burn, will exert a very great destructive action on the cancer cell. The question arises why uniformly good results should follow the treatment of skin cancers, and almost as uniformly poor results be obtained in the treatment of cancers in only slightly deeper tissues. The problem involved is the immediate basis of the experiments to be described in this paper."

It was a recognition of the question so clearly stated above that impelled us to start our clinical experiments some two years ago, with a view both to increasing skin tolerance, and, if possible, finding some way to prevent or overcome the undesirable sequelae of massive dosage. With increased skin tolerance established, it may still be found that the increased dosage possible will not solve the problem, but that other measures, such as employing superheated air to induce a pronounced lymphocytosis,[4] will have to be used in addition to the roentgen ray and the ultraviolet ray. Again it may be found that the larger doses of a softer ray,[2] made possible by increasing the skin tolerance, will help in the solution. It is admitted by most roentgen-ray therapists that the use of soft unfiltered rays in skin cancer gives results at least equal, if not superior to the hard filtered rays, and the smaller dose of softer rays—larger than formerly possible but still much smaller than the dosage of hard filtered rays—while producing more local reaction, would not cause such a heavy reduction in the lymphocyte count, with the concurrent increase in susceptibility. This has been shown by Amoss, Taylor and Witherbee.[5] No matter from what angle the problem is viewed, the breaching of the stone wall of skin tolerance will allow entrance to new research fields.

A search of the literature serves only to pile up evidence for and against any given hypothesis, without definite proof either way. Any single set of experiments, no matter how valuable they may seem to be, can hardly hope to prove or disprove any given theory as to the exact action of the roentgen rays upon the body tissues. Until the evidence from numbers of research centers is in, and unless such evidence shows a preponderance of weight upon one side or the other, the explanations put forward may be said to be unproven as yet. This being the present status of the question as to why, exactly, certain reactions do follow certain doses of the roentgen rays, the proof as to how ultraviolet light antidotes any of these effects, or could operate in breaking up the cycle of changes following such massive dosage, could not be given (except clinically) even were very much more exact knowledge of the action of the actinic rays at hand than is the case.

The literature upon ultraviolet light, while fairly voluminous, is mostly clinical, and presents all the usual difficulties when attempt is made to draw conclusions from a sifting of the evidence. Edgar Mayer,[6] in a remarkably complete critical review of the literature on sunlight and artificial light in tuberculosis, most of which deals with ultraviolet light (his list of bibliographic references, printed in smaller type than the text and closely spaced, extends over more than thirteen pages and shows a wide search) gives some of his conclusions as follows:

"It is evident that we have yet many problems to solve. Some of these are: (1) The question of the exact mode of the formation of *pigment* and the actual rôle of this substance. (2) The proof of any specific powers possessed by pigment. (3) The ability or inability of pigment to change short rays to longer and more penetrating ones. (4) The relation of pigment to prognosis and lymphocytosis. (5) The ability of pigment to set up focal reaction in tuberculosis.

"We require many more experiments to show the exact *penetrating powers* of the various rays, and additional data in relation particularly to the effect of violet and ultraviolet rays upon tissues, both healthy and

diseased, and upon bacteria, especially *in vivo*.

"More experiments are needed to compare the effects of the ultraviolet rays with those of the red and ultrared rays, and many more comparative results between high and lower altitudes are necessary.

"From clinical experience with surgical tuberculosis, evidence points to the greater value of the ultraviolet rays, although it appears that the heat rays may also aid.

"Insufficient comparative and statistical studies upon patients, especially upon those with pulmonary disease, leave much to be desired.

"Much more knowledge must be had experimentally of the effect of light upon non-tuberculous conditions."

Again: "The action of light on ferments and so-called 'antibodies' and other constituents of the blood, as well as its means of influencing the deeper organs, is mostly a matter of speculation up to the present. Its effect upon protoplasm is not well understood.

"The more important ultraviolet rays that affect cells, toxins, bacteria, ferments, etc., are present in the quartz mercury lights but absent in the sunlight as it reaches us."

The conclusion that the shorter the wave-length of ultraviolet the more soluble it is in protoplasm and the more powerful it is in its effects is expressed also by Bayliss[7] in his conclusions after his discussion of the action of light. Kober,[8] in a spectrographic study of amino-acids and polypeptides, and Harris and Hoyt,[9] in a study on the possible origin of the toxicity of ultraviolet light, have added some evidence to that already known, but much more is needed. All the ultraviolet work, up to a very recent date, was done with the iron core arc, tungsten core arc, and the old type quartz mercury vapor arc. The ultraviolet-ray apparatus is going through much the same evolution that the roentgen-ray apparatus has gone through; from the static with a capacity of one or a very few milliampères through the tube to the modern high tension transformer and Coolidge tube outfit, capable of answering almost any demand made upon it.

The old carbon arc gave limited quantities of ultraviolet light of the longer wave-lengths. The various improvements as different minerals were substituted in the composition of the carbon, resulted in greater quantities, but the wave-lengths remained comparatively long, and the constant attention demanded, the noise, heat, their unsteadiness and their many mechanical faults, kept them from being extensively used. With the advent of the quartz mercury vapor lamp with its spectrum reaching into the shorter wave-lengths, and nearly all the faults of the older arc lamps eliminated, a distinct move forward was made. A new type of quartz mercury burner has been on the market about a year. Spectrum tests just being finished at the University of Chicago would indicate that its spectrum goes to the limit of quartz transmission, or about 1,800 Angström units. No intensity tests have been made, so far as we have been able to determine, but judging by its clinical effects it will probably be found to give a great volume of the shorter wave-length rays. With the new burner an erythema can be produced in about one-third of the time required by the older quartz mercury type. Air and water cooled lamps of old and new quartz mercury type are in constant use in our clinic, and both are efficient in increasing skin tolerance to the roentgen rays when used properly. By a series of experiments with the effects of ultraviolet light from an iron arc unscreened and filtered through various substances, such as clear glass, red glass, Wood's ultraviolet glass, picric acid, etc., upon the leukocyte count in rabbits, Clark[10] has shown that the shorter ultraviolet rays are the ones producing the leukocytosis, and that the longer ultraviolet wave lengths, in common with nearly all the longer light wave lengths, produce a fall in the leukocyte count. It would seem, therefore, that the use of the quartz mercury lamp, which gives much shorter wave-lengths than any of the arc lamps, would be preferable wherever a high leukocyte count or a marked dermatitis is to be desired. From a clinical standpoint, it is a matter of common knowledge among extensive users of the ultraviolet light that this physical remedy possesses remarkable value in a wide range of conditions. The

rapidity with which certain morbid conditions can be modified is illustrated by Case V, which illustration could be duplicated in extenso from our case records, did space permit. It is a routine practice in our clinic to prescribe general ultraviolet radiations in all suboxidation states and all so-called toxemic conditions. Results from its use in metabolic disorders are usually prompt and vigorous. Its anodyne properties in such conditions as gastritis, gastric and duodenal ulcer and many malignancies have been, and still are, an unexplained mystery to us. Diabetes seems to be the only metabolic derangement where actinotherapy cannot be used. In any dosage whatever, it causes a diabetic to show, promptly, symptoms duplicating surgical shock, or even anaphylaxis. The best explanation of this that we have seen is one given by McCaskey,[11] than whom, certainly, very few men in this country have had more experience in actinotherapy or have kept closer metabolic check upon their cases. Discussing diabetes he states:

"Let us for a moment discuss the constitutional disease, diabetes. Here we have an endocrin breakdown. We now know that ultraviolet light affects the acetone components of metabolism by increasing or activating their decomposition to gas formation (Schanz, F., *Arch. f. d. ges. Physiol.* (Pflüger's) 1918, pp. 170, 646.) It has been my observation that in the application of quartz ultraviolet light to the human body, the individual's oxidation index is invariably raised to a higher percentage. For instance, a patient free from diabetes, whose urine reveals a proportion of urea nitrogen to total nitrogen of 50 per cent, will, after the application of several months' treatment with quartz ultraviolet light, have this proportion raised 20 to 30 per cent. Ordinarily there exists an idea that diabetes is a disease of suboxidation. This idea is a fallacy; it is not borne out by the chemical facts, for invariably the urine oxidation index of this type of endocrine breakdown is above 85 per cent urea nitrogen to total nitrogen. My last two diabetic cases revealed a peak of 89 per cent, and 88 per cent respectively. As quartz ultraviolet light stimulates the oxidizing power of the synthetical forces of the body and as, in my judgment, diabetes is a superoxidization process, treatment with ultraviolet light cannot be administered at all, so long as the patient's metabolism is not in chemical equilibrium. During the past four years of my work with ultraviolet light in constitutional disorders, I have tried it repeatedly in diabetes, from small to moderate doses. Always the same result occurred, namely, the patient reacted poorly and gave every indication of increased toxic distress similar to anaphylactic shock. As a result of these detrimental toxic experiences, I, today, do not administer ultraviolet light to a diabetic.

"To summarize: A technique for the better coordination of the kinetic bodily forces may be divided into two parts, one relating to internal, the other to external technique.

"Internal technique involves the accurate quantitative knowledge of the constituent chemical ingredients of the blood and urine and a heart electrocardiogram. It further involves the regulation of the chemical food intake to the chemical outgo, so that a nitrogen equilibrium is maintained.

"The external technique involves the treatment of the body skin surface with quartz ultraviolet light, the absorption of which stimulates tissue metabolism. In toxic quantities quartz light produces anaphylactic shock. With the exception of diabetes, however, quartz light results in a raising of the factor of tissue vitality, or, it might be termed, of the patient's prophylactic resistance to disorders of nutrition, whether of acidosis or other low oxidation states."

So much for the ultraviolet constitutional effects. The conjoint use of the ultraviolet and the roentgen ray was suggested to us gradually by a comparative study of both their local and general effects, and by the ease with which a *beginning* roentgen-ray dermatitis could be cut short and, clinically at least, cleared up by vigorous actinotherapy. And the ultraviolet therapy in these cases, to be effective, must be vigorous. It is effective even after ulcer formation begins, provided it is used before masses of cicatricial tissues have formed. Once these have formed, the case should not be expected to respond to actino-

therapy alone. Surgery, radium, diathermia, or some other means of softening or eliminating the scar tissue must precede the application of the ultraviolet light. We have seen it stated that the use of the actinic rays might be followed by xeroderma pigmentosum or skin cancer. We have never been able to authenticate a case of this kind from heavy actinic doses. No doubt there have been cases due to irritation from the actinic ray in the sunlight (which is of the longer wavelength—never below 2,910 Ångström units, and of no great intensity as compared to quartz-burner intensity) but in this case we would state that clinical experiences lead us to believe that the skin may react to the actinic ray irritation somewhat as it acts when telangiectases form from roentgen ray, i.e., that it is more apt to form from small doses over considerable area, often repeated, than from heavier dosage. We have been cautioned by prominent roentgen-ray therapists that it was against all the rules of the game to superimpose an actinic erythema upon a skin that had already received a dermatitis dose of roentgen rays. We can only answer by stating the clinical fact that we have been doing it for a number of years without a single depilation occurring, or symptoms which would indicate that a dermatitis had occurred, and have greatly exceeded dosages which, before the use of this method, regularly gave us a dermatitis. These well-meant cautions have had the effect of causing us to treat a few hopeless cases first and wait for months before increasing the dosage proved safe in those cases. The result is that we have pushed the dosage only to the figures given in the appended cases. Whether these dosages can be much extended is a problem for future research. We have, until now, been handicapped by the fact that our laboratory has been running overtime on routine work and could not take on any research work for us along this line; but preparations are being made for expansion, and facilities planned for the doing of a great number of experiments by which we hope to prove on a large scale the value of this combined technique, and set out the limits of safety.

The *x*-ray outfit used in these cases was a Wappler, King model, Coolidge tube, medium focus; and the constant factors were: Spark gap, 9 in., (except splenic area, Case II, where it was 10 in.); target skin distance, 8 in.; filter 6 mm. aluminum, 2 mm. leather; ma. in tube, 5; time variable, as given. The ultraviolet outfits were of the quartz mercury vapor type both air cooled and water cooled. The roentgen-ray treatments were given by the medical officer roentgenologist and 2 competent *x*-ray technicians, and every factor checked up by each of us. The timing was done by an interval timer checked by three standard watches set in synchronism. The spark gap was always at least that given, and broke over several times, with the parallel gap set at 10 and 11 in. respectively. A series of 27 skin areas tested on control subjects of approximately the same ages and complexions as the cases cited (areas were on back between shoulder blades) gave the time necessary to produce a first degree erythema with the 9 in. gap, and other factors used as an average of 17½ ma.m.

As the ultraviolet technique was the same in all cases, the detailed dosage will be given only in the first case. The essence of the technique is to prepare the skin area to be treated by the roentgen rays by a series of actinic-ray erythemas produced as rapidly as the preceding one begins to die out, and repeated until heavy tanning takes place, or, in case the subject will not tan, for approximately four weeks; and at the same time give general ultraviolet radiations (not necessarily so severe, but as strong as comfort of patient will allow) for the constitutional effect. When it is decided that the area is prepared sufficiently, allow the last actinic erythema to fade out, and then give the roentgen-ray treatment. On the same day, but *after* the roentgen-ray treatment, give at least as much ultraviolet exposure as was given at the last previous ultraviolet treatment over the area treated by the roentgen rays. Also keep up the general ultraviolet exposures. Repeat the application of the ultraviolet in the same or slightly increased dosage over the roentgen-treated area about every forty-eight or seventy-two hours, as the actinic reaction indicates, until that area has had at least 3 good

actinic exposures, and then allow all actinic erythema to die out, so as to be able to detect the roentgen erythema which will come up later if it is to appear. In practice we cover a small central area after 2 or 3 actinic treatments, and keep up the ultraviolet applications to all the rest of the area for a period of three weeks, using the small covered area as a control for the *x*-ray erythema.

CASE I. Male, aged thirty-seven, American, Sergeant, U. S. Army.

Family History. Negative.

Personal History. Negative.

The first appearance of a tumor size of a hickory nut on left forearm in October, 1918. This was removed in March, 1919, at Fort Riley, Kansas.

Patient was sent to Camp Upton in December, 1919. Diagnosis, recurrent tumor, left forearm. This was removed December 17, 1919, being the second operation. A specimen was sent to the laboratory for pathological report.

Diagnosis. Sarcoma, mixed cell type. Tumor recurred rapidly after second operation.

Patient admitted to Army General Hospital April 27, 1920. Tumor size of cocoanut on the ulnar aspect of left forearm.

X-Ray Report (April 27, 1920). Stereo of left forearm, upper third including elbow shows growth of soft tissue not involving the bone. From the lateral plates the upper third of radius is bowed forward as if from pressure in this region. There is a slight amount of thickening of the periosteum of the ulna in this region. The cortex of both bones is intact, the elbow is negative, as are the plates of the chest.

May 11, 1920. Specimen from epitrochlear gland to laboratory.

Gross Examination. Small mass 1 cm. long by ¾ cm. thick.

Microscopical Examination. Small amount lymphoid elements, being a small lymphoid follicle at one edge of section. Main structure of section is a loose mass of cells, large spindle cells predominating, with numerous large round cells. Also connective tissue and newly formed blood-vessels. No giant cells.

Diagnosis. Sarcoma, mixed cell, large spindle cells predominant; not a lymph gland.

May 29, 1920. *X*-ray of chest. Stereo of chest shows slight retraction on lower right lateral aspect of chest wall. Heart and chest otherwise negative except for four circular areas of consolidation which give the typical snowball appearance of metastasis of sarcoma.

Three areas appeared after the last plate was made and one, which was present in the last plate, was not more than a third of its present size and had not taken on any characteristic appearance at that time. It was located in the lower part of the hilum where small areas of consolidation are often found. No special significance could have been given it then. Small accumulation of fluid at the base of left chest which was not present at the previous examination.

Diagnosis. Sarcoma of left forearm with metastases of chest. Patient referred to physiotherapy service May 27, 1920, at which time preliminary treatment was started and the photograph which accompanies this article was taken.

Operation Report. (May 29, 1920.) Sarcoma left forearm with axillary and pleural involvement by metastasis.

Operation. Amputation middle third humerus; dissection of axilla. Curved incision 12 inches long from middle of pectoralis major along course of cephalic veins to lower third of upper arm. Tendon of pectoralis major divided ¾ inches from its insertion and turned back. Axilla dissected, removing all fat and glands. Axillary vein dissected clear, exposing brachial plexus. Flap dissected on upper arm (rachet) and brachial artery and vein, cephalic and basilic veins tied. All nerves injected with alcohol and cut by fishtailing after pulling down. Muscles cut through and bone sawed, periosteum removed off cut edge, triceps sewed to biceps over bone end by interrupted sutures, wound closed. Major Jones.

PHYSIOTHERAPY TREATMENT

NOTE. In giving the ultraviolet exposures, to save space, the air cooled ultraviolet lamp will be designated by "A" and the water cooled ultraviolet lamp by "W." The time in minutes will be the first numeral, X will mean "at," and the following numeral will be the number of inches from target to skin, or in the case of contact exposures with the water cooled

lamp the letter "C" will denote contact; thus 2 × 18-A will mean two minutes at 18 inches with the air cooled lamp and 10 × C-W will mean ten minutes at contact with the water cooled lamp, etc.

Date	*Region Irradiated*	*Exposure*	*Ultraviolet Skin Reaction*
May 27	Over metastases	6 × 1-W	Mild erythema
May 28	Over all sides chest	2 × 22	Mild erythema
	Operation		
June 15	Over metastases	6 × 1-W	Mild erythema
June 15	General over chest	2 × 22-A	Mild erythema
June 18	General over chest	2 × 22-A	Mild erythema
June 20	Legs, front and rear	2 × 22-A	Mild erythema
June 21	Over all chest	3 × 22-A	Mild erythema
June 21	Over metastases	4 × 1-W	Mild erythema
June 22	Legs, front, rear	4 × 22-A	Mild erythema
June 23	Over chest	4 × 22-A	Mild erythema
June 24	Over metastases	9 × 1-W	Good reaction
June 25	Chest, legs, all sides	3 × 22-A	Mild reaction
June 26	Legs	5 × 20-A	Good reaction
June 26	Chest	4 × 20-A	Good reaction
June 27	To metastatic areas	10 × C-W	Heavy reactions
June 28	Chest	8 × 20-A	Good reaction
June 28	Legs	4 × 20-A	Good reaction
June 29	Chest	7 × 20-A	Good reaction (tanning well)
June 29	Legs	9 × 20-A	Good reaction
June 30	Chest	10 × 20-A	Mild reaction
June 30	Legs	8 × 18-A	Mild reaction
July 1	Legs	8 × 18-A	Mild reaction
July 1	Chest	10 × 18-A	Mild reaction
July 2	Chest	12 × 18-A	Mild reaction
July 2	Metastases	10 × −C-W	Mild reaction
July 5	Metastases	10 × −C-W	Mild reaction
July 5	Chest	8 × 15-A	Mild reaction
July 6	Chest	10 × −15-A	Very slight reaction (Acct. deep tan)
July 6	Legs	8 × 18-A	Very slight reaction (Acct. deep tan)
July 7	Metastases	11 × C-W	Good slight reaction
July 8	Chest, legs	10 × 18-A	Mild reaction
July 10	Chest	12 × 18-A	Mild reaction
July 10	Metastases	12 × −C-W	Mild reaction
July 12	Chest	12 × − 18-A	Good reaction
July 12	Legs	10-18-A	Good reaction
July 13	Chest	12 × 18-A	Mild reaction
July 13	Legs	10 × 18-A	Mild reaction
July 15	Metastases	15 × 1-W	No reaction
July 18	Chest	15 × 18-A	None
July 19	Chest	15 × 18-A	None
July 20	Chest	15 × −16A	None
July 20	Legs	15 × 16-A	None

Area of experiment 6 × 4½ inches on antero lateral aspect of lower right chest, over the largest double metastasis. Diagrammatic reproduction of area follows.

1	A	4	D
July 30 *X*-ray dosage 45 ma.m. to areas 1 and A		August 2 *X*-ray dosage 25 ma.m. to areas 4 and D	
10 × C-W July 30 10 × 20-A July 31 10 × 1-W Aug. 2 Etc. See below	No after treatment with ultraviolet	Ultraviolet same as square Number 1	No after treatment with ultraviolet
2	B	5	E
July 30 *X*-ray dosage 62½ ma.m. to areas 2 and B		August 4 *X*-ray dosage 75 ma.m. to areas 5 and E	
Ultraviolet same as square Number 1	No after treatment with ultraviolet	Ultraviolet same as square Number 1	No after treatment with ultraviolet
3	C	6	F
August 2 *X*-ray dosage 50 ma.m. to areas 3 and C		August 4 *X*-ray dosage 75 ma.m. to areas 6 and F	
Ultraviolet same as square Number 1	No after treatment with ultraviolet	Ultraviolet same as square Number 1	No after treatment with ultraviolet

The lettered areas were not treated with ultraviolet *after* the *x*-ray exposures were made. The numbered areas were treated with ultraviolet as follows:

On the day of *x*-ray exposures and immediately after the *x*-ray had been given:

Same day	10 × C-W
Next day	10 × 20-A
Third day	10 × 1-W
Sixth day	15 × 1-W
Ninth day	15 × 1-W
Tenth day	12 × 16-A

In an ordinary case with a moderate overdose of *x*-rays, the subsequent ultraviolet treatments would be stopped at the end of six or seven days, as the *x*-ray erythema usually comes up in from eight to fifteen days. In this particular case, we carried the ultraviolet treatment to ten days, and used the lettered areas as a control to watch for the *x*-ray erythema. We fully expected to produce an erythema on the lettered areas, and were trying hard to prevent it on the numbered areas. We were pleasantly surprised when no erythema resulted upon either the lettered or numbered areas. In addition to the radiation directly through the metastases, the two larger ones were treated by crossfiring, from four angles, using a 50 ma. m. exposure. A marked *x*-ray dermatitis appeared in the left axilla, the hair coming out and ulceration starting on the skin of the stump where we had neglected to tan the skin of both areas, on account of the dressings on the stump. This was not from direct exposure of these areas to the *x*-rays, but was caused by the crossfire rays emerging from the body at this point. It quickly cleared up under a few ultraviolet treatments. In addition to the *x*-ray experiment upon areas F and 6, and to test the irritability of the skin after these massive dosages, a capsicum plaster was applied. When no result was evident in twenty-four hours, a second, and later a third plaster was applied to these same areas before a mild blister resulted. A control gave a blister overnight.

Location of metastases has been marked on the chest wall on the photograph. Under this treatment the metastases rapidly

dropped out of the picture. Patient's general condition improved from the start. He was transferred to a hospital nearer his home a short time after his course of treatment was finished, but continued to improve. He visited our clinic last month (May, 1921). He has regained his normal weight and says he has, and looks to have, rugged health. He is developing a hard mass in his left calf which is probably sarcomatous in character, and has a small suspicious area in the lower posterior chest, which is not one of the original metastases. This area was not in the heavily rayed portion of the chest. He has been advised to return at once for a full course of treatment, and is taking the necessary steps to be admitted as a patient to this hospital. We hope to control these metastases as the others were controlled.

CASE II. Male, aged twenty-nine, American, chauffeur.

Family History. Negative. No cancer, tuberculosis or insanity in family.

Personal History. Negative. Habits good. Smokes cigarettes.

Drafted May 18, 1918. Discharged March 15, 1919. First noticed sore on lower lip, left side, December 10, 1918, in Beautesart, France. Wassermann done at this time negative. Sore started as small pimple, ointments applied. Healed and broke open at intervals until his discharge, gradually growing larger. Discharged at Camp Dix and immediately consulted his family physician. Wassermann again negative. May 20, 1920, excision of growth was done. Remained in hospital one week and returned home. Three weeks later gland in neck removed. Wound broke down after five months, and after consulting his physician again, he was treated until February, 1920, when he was referred to another hospital, where he received 2 applications of radium, three weeks apart. Relief for some months and then pain and swelling started again. Admitted to this hospital December, 1920. Condition as shown on April 2, 1921, when he was referred to our clinic for treatment. Ultraviolet treatment in preparation for roentgen-ray treatment started, although results were very problematical, due to degree, age and previous operations. At end of ten days urgent pressure symptoms developed with a rapidity which made it inadvisable to defer roentgen-ray treatment, and after consultation with several surgeons it was decided to give him the maximum dose although he had not had the areas properly prepared. On April 11th, he received 75 ma. m. over metastatic tumor in left occipital triangle; on April 12th, 75 ma. m. over primary growth area and over metastases in left superior carotid triangle; on April 13th, 75 ma. m., over metastases in right occipital and right superior carotid triangles; and on April 14th, 75 ma. m., over metastases in region of left parotid gland. On May 2nd, he received 75 ma. m., over left parotid region again; on May 9th, 75 ma.m., over night submaxillary triangle. In spite of these dosages with their crossfire rays emerging in some cases in another treated area, and his insufficient preliminary ultraviolet preparation, no dermatitis resulted. On June 11th, 13th and 15th, he again received 75 ma. m., over the left parotid, right submaxillary and primary areas respectively. His ultraviolet was kept up regularly. He is still alive, but failing, and his latter treatments were more to satisfy him than in hope of doing any real good. His beard is still in place and pains him when it is pulled. Blood count ranges from 6,624,000 reds to 4,080,000 and whites 6,600 to 7,200. Hemoglobin 65 to 73 per cent, differential small mononuclears 16 and 17 per cent, large mononuclears 3 and 4 per cent, eosinophiles 1 and 2 per cent, neutrophiles 77 per cent.

CASE III. Male, aged thirty-four, Italian.

Diagnosis. Osteosarcoma with metastases.

Family History. Negative.

Personal History. Negative. Smokes cigarettes.

May, 1920, had pains more or less generalized over body, but especially over right clavicle. In July, 1920, noticed lump over right clavicle. Treated at home until October, 1920, when he was admitted to a hospital in New York City, remaining there until February 3, 1921, when he was admitted to this hospital. Condition on being admitted: Cast from 7th cervical to junction between middle and lower third

of the tibia. Report of consulting orthopedist (February 4, 1921):

"There is a large, spherical mass attached to right clavicle. Condition is probably a sarcoma with metastases in spine and chest. Liver also enlarged, edge being felt about 12 cm. below costal margin. Condition inoperable. Request that *x*-ray and summary of history from the New York hospital be obtained."

In December, 1920, patient also had pleurisy with effusion while in the New York hospital. Patient was sallow, anemic, emaciated, and could not be removed from his cast, which shell extended from neck to heel and partly up the sides of the body. Careful lifting and turning were required to get him out of his cast for treatments, and at first this caused him great pain. On April 11, 1921, was given preliminary ultraviolet treatment, and then 75 ma. m. in. over each of the two most painful areas on spine. On April 12th, the primary growth at sternal end of right clavicle received the same dose; on April 13th, the metastases in region of sternal end of left clavicle received 75 ma. m. in., and on April 14th a cluster of metastases at costal extremities of 6th, 7th, 8th and 9th ribs received 75 ma. m. in. The roentgen-ray plate showed all these metastases except that clear plates of the spinal lesions were impossible to obtain. Pain began to lessen in all areas thirty-six to forty-eight hours after the roentgen-ray treatment was given. On April 28th, after patient had complained of constantly increasing pain in splenic area, and a hard mass could be made out by palpation, he was given 90 ma. m. with a 10 in. back-up spark over this area. The pain lessened at once, but persisted for some two weeks, when it also disappeared. No roentgen-ray sickness resulted from this dose, and Figure 3*a* shows the condition of the hair over this area, showing that on the sixteenth day after the *x*-ray dose, when this plate was taken, the skin of the abdomen could be pulled out an inch or more by tension on a dozen hairs. This test was made daily for six weeks after the administration of the *x*-ray dose, and showed a healthy condition of the hair follicles all the way through. Figure 3*b* of the same case shows what happened when he was given the usual time and distance in one of his preliminary actinic ray treatments, but when a brand new burner had been substituted, and the attendant overlooked the notice on the lamp ordering exposures cut in two until the new burner could be standardized. The whole exposed area exfoliated in large strips, and small blisters were produced in the center where the intensity was greatest. In spite of his poor condition (his blood picture showed a condition almost exactly simulating pernicious anemia) he became so much better after the *x*-rays were administered that he was able to get out of his cast into a wheel chair by his own efforts and propel himself around the ward. His anemia is gradually taking him down again, and it is only a question of time for him, in spite of transfusions or other expedients. The primary growth has retrogressed one-third in size, and the nodules on the ribs have practically disappeared. He is too ill to move to the roentgen-ray department for further plates.

Case IV. Male, aged fifty-seven, Irish, merchant marine.

Diagnosis. Basal cell epithelioma.

Family History. Negative.

Two and one-half years ago a small sore appeared. Treated with various ointments, healed, but broke open again. Says there was no mole in that locality. Sore gradually grew larger until it reached the size and appearance shown. This case is shown only because of his complexion, his skin being of the type that blisters readily, but will not tan under the strongest ultraviolet-light exposures. After preliminary erythemas from actinic rays, under which the lesion almost disappeared, he was given 75 ma. m., and parotid and carotid regions are now being prepared for prophylactic raying, on the remote possibility that a metastasis might appear later. He was given the *x*-ray treatment on May 31st, and up to June 25th had shown no signs of erythema.

Case V. Male, aged twenty-nine, American.

Diagnosis. General paronychia.

Family History. Negative.

Personal History. Negative, except that

patient was gassed in 1918. A short time afterwards he developed the pustular condition of the nails which progressed in spite of all treatment. When he came to our clinic a year ago he had lost, or had had removed, every finger and toe nail, and pus was exuding from the matrix. The *x*-ray plate showed a periostitis of every terminal phalanx. He had been given vaccines, both stock and autogenous, had had applications of iodoform and glycerine for months, etc., and was finally referred to us for treatment. Every one of our air cooled actinic-ray lamps was running overtime on serious cases, but after a few days a place was found for him on one of the water cooled lamps, and he was started on *local* ultraviolet treatments. He made no improvement until a vacancy occurred on one of the air cooled lamps (ultraviolet) when he was given *general* treatments in addition to the local ones. Improvement was manifest by the fifth day, and in seven and a half weeks he was discharged from the army and went home. He kept in touch with us by writing at intervals, and after a lapse of eight months he wrote that his hands and feet were perfectly well, and that he had new nails coming in on all fingers and toes; but he wanted to know why they were so brittle. This case had received no treatment for months before he came to our clinic, and received no other treatment at the hospital at any time except the actinotherapy outlined. An *x*-ray plate taken the day before he left showed no signs of a periostitis.

SUMMARY

In the human organism the epidermis is the natural covering which acts as a defense against certain stimuli in which the individual is immersed. Individuals have constantly been exposed to the sun's actinism, so that, a priori, the skin is the naturally provided filter against such actinic effects as must be excluded from the body, but it is at the same time permeable to those actinic effects which act as adjuvants in fostering the physiological unity of the individual.

The tanning or sun-burning of the skin may be accomplished more rapidly and under more perfect control in the clinical theater by the use of scientifically elaborated apparatus, whose function it is to duplicate with intensity the therapeutically useful actinic spectrum.

The trial and error of empiricism has established that an effect of clinically induced "ultra sun-burn" is such as to provide an epidermal pigmentosis. This newly induced epidermal pigmentosis so reacts that the area involved, when exposed to relatively soft *x*-rays, permits of the assimilation by that part of a greater quantity of physiologic roentgen radiation, at the same time precluding the physiologically detrimental effect that would otherwise be produced on an area of skin unexposed to intense actinism.

An extremely important principle is discovered; the principle that nature has provided the guide for offering a protective mechanism whereby spectral phenomena closely allied to ultraviolet activity, or *x*-rays, can exert very helpful and stimulating influences without exercising deleterious effects such as are produced without proper preparation.

The application of this fundamentally important principle is at once obvious. It precludes the necessity for elaborating expensive and impractical apparatus to generate an unnatural radiation in the treatment of disease. For with the unnatural *x*-ray radiation, unnatural filters of copper, aluminum and zinc are made necessary. In effect, ultraviolet treatment of an area provides the natural means that the laboratory experimenter endeavors to secure through the use of copper and other unusual metallic elements.

The essential feature of this clinical research is to point out that ultraviolet and *x*-ray radiations are physiological complements. The one may be used in symbiosis with the other. That is, the ultraviolet applied first renders the area more resistant to the subsequent radiation with the roentgen rays. The roentgen rays applied first may produce a dermatological change injurious to the organism; but the effects of that injury can be alleviated or entirely neutralized by applying secondarily the

ultraviolet radiation. From this foundation it is adduced that the ultraviolet greatly extends the previous limits of *x*-ray efficacy in the treatment of disease.

Hence the conclusion of an empirical research is obviously the empirical restatement of the research itself and carries with it the single conviction that the clinical trial of the method presented accomplishes more than speculative conjecture based on hypothetical presumptions.

BIBLIOGRAPHY

1. Hall, C. C. and Whipple, G. H. Roentgen ray intoxication: Disturbances in metabolism produced by deep massive doses of the hard roentgen rays. *Am. J. M. Sc.*, April, 1919.
2. Denis, W., Martin, C. L. and Aldrich, M. A study of the relative toxic effects produced by regional radiation. *Am. J. M. Sc.*, Oct., 1920.
3. Murphy, J. B., Hussey, R. G., Nakahara, W. and Sturm, E. Studies on *x*-ray effects. VI. Effects of the cellular reaction induced by *x*-rays on cancer grafts. (From the laboratories of the Rockefeller Institute for medical research.) *J. Exper. M.*, xxxiii, No. 3, 301.
4. Murphy, J. B. and Sturm, E. The lymphocytes in natural and induced resistance to transplanted cancer. *J. Exper. M.*, 1919, xxix, 25. Effect of stimulation of the lymphocytes on the rate of growth of spontaneous tymors in mice. *J. Exper. M.*, 1919, xxix, 31.
5. Amoss, H. L., Taylor, H. D. and Witherbee, W. D. Effects of large doses of *x*-rays on the susceptibility of the monkey to experimental poliomyelitis. *J. Exper. M.*, 1919, xxix, 115.
6. Mayer, E. Sunlight and artificial light therapy in tuberculosis. A critical review. American Review of Tuberculosis, v, No. 2.
7. Bayliss, W. M. Principles of General Physiology. New York, 2nd ed., p. 578.
8. Kober, P. A. Spectrographic study of amino acids and polypeptides. *J. Biol. Chem.*, 1915, xxii, 433.
9. Harris, F. I. and Hoyt, H. S. The possible origin of the toxicity of ultraviolet light. *Science*, 1917, xlvi, 318.
10. Clark, J. H. The action of light upon the leukocyte count. *Am. J. Pub. Hyg.*, 1921, i, No. 1, 39.
11. McCaskey, D. Quartz ultraviolet therapy and kinetic energy. *N. York M. J.*, Dec. 27, 1919

TREATMENT BY RADIUM OF NASAL POLYPS*

BY HORACE R. LYONS, M.D.

Section on Otolaryngology and Rhinology, Mayo Clinic

ROCHESTER, MINNESOTA

THE underlying cause of nasal polyps is inflammation which involves either the nasal mucous membrane or an accessory nasal sinus and, in some cases, both. The fact that inflammation, due either to irritation as in vasomotor changes, or to suppurative conditions, usually is a cause of nasal polyps, has a direct bearing on the treatment, in that simply removing the polyp will not affect the underlying inflammatory process which must be eradicated. The pathological condition associated with the polyp, is usually disease of a sinus. In the majority of the cases, the anterior and posterior ethmoid sinuses are affected, although the inflammatory process may involve any or all of the other sinuses.

Nasal polyps may be divided pathologically into five groups: (1) Myxomatous, (2) adenomyxomatous, (3) fibromyxomatous, (4) adenofibromyxomatous, (5) fibromatous.

Group 1. Myxomatous polyp is the type most commonly found in the nose. Such polyps may occur at any age, but are most often found in middle-aged persons. At examination the tumor appears large, soft, and water-logged. It may be spherical or pear-shaped with a neck or pedicle which is attached to the mucous membrane over a sinus. It bleeds very freely when touched and is movable.

Group 2. Adenomyxomatous and myxomatous polyps are identical clinically and are differentiated only by microscopical examination. This reveals that an adenomyxomatous tumor has, in addition to the structure of a myxoma, a number of glands scattered throughout the tissue. Regeneration of myxomas and adenomyxomas is very rapid and these

*Read at the Seventh Annual Meeting of The American Radium Society, St. Louis, Mo., May 22–23, 1922.

types tend to recur over a larger area than that of their original appearance.

Group 3. A fibromyxomatous polyp, on observation, has a distinct water-logged appearance, but, unlike the polyps of Groups 1 and 2, is firm and bleeds less freely when touched. It is much more resistant to a probe than the others, and is usually attached to the mucous membrane over one of the sinuses. Microscopic examination shows the structure of a myxoma with a varying amount of fibrous tissue throughout. This tumor usually does not recur over an area increasingly large.

Group 4. An adenofibromyxomatous polyp clinically resembles a fibromyxoma and is differentiated from it only on microscopic examination, which shows the structure of a myxoma with fibrous and glandular tissue throughout. This type of tumor is similar to fibromyxoma in recurrence and reaction to radium.

Group 5. A fibromatous polyp is a clinical entity. It is hard, and may or may not have a pedicle. It offers considerable resistance to the probe on examination and does not move freely. Fibroma is more likely to be single than multiple. Clinically, there are two types, the hard, or so-called fibroma durum, and the soft fibroma, both of which microscopically are seen to consist of fibrous tissue only. Fibromas are the least common of all nasal polyps.

TREATMENT

All possible methods of medical and surgical treatment have been attempted and, as yet, a definite procedure that will effect permanent cure has not been found. The use of radium was introduced about three years ago in an effort to aid operative measures in effecting a cure, or, at least, in delaying recurrence. The operative procedure will not be discussed, except to say that in the Mayo Clinic it has been found that rather radical removal of the tumor is not sufficient to produce the desired effect and radical exenteration of the involved sinuses is necessary. We attempt to eradicate the suppurative disease of the sinus as well as to remove the polyp. It has also been found that simply removing the polyp at its point of attachment is insufficient, because the polyp is likely to recur in the surrounding mucous membrane. Therefore, a wide excision of the membrane around the point of attachment is necessary.

Radium. The use of radium for nasal polyps postoperatively was undertaken in the Mayo Clinic three years ago in the hope that radium would stimulate the production of fibrous tissue in the recurring polyp and thus make a second operation more successful. This is based on the fact that the more nearly a polyp pathologically simulates the fibroma, the more easily a complete cure is effected by removal; in myxomatous polyps it is very difficult to effect a cure.

This study is based on a series of 55 cases of nasal polyps in which radium was used postoperatively 111 times to total 14,892 mgm. hours. At first, radium burn was very much feared, particularly because data were not found in the literature with regard to the use of radium in nasal polyps, and only a 25 mgm. tube of radium was used postoperatively for one hour. Burns did not result, and since more radiation was deemed necessary, a 50 mgm. tube of radium has been used for from two to three hours at intervals of one week, the first treatment being given on the second or third day following operation. In 3 cases, as much as 1,000 mgm. hours of radiation has been directed to the point of attachment of the polyp. The radium is screened by a thin silver tube with a small ring at one end to which a string is attached. The silver tube, in turn, is covered by a sterile rubber finger-cot. The tube of radium is embedded in the center of the area most active in the production of the polyps and the string is attached to the cheek by adhesive tape. The use of 150 mgm. hours of radiation postoperatively at one-week intervals can be continued for an indefinite time without causing a burn. In the cases herein reported, radium was used as often as five times; complications due to the radium did not result.

The ultimate results in a few of the 55 cases are unknown because some of the patients did not remain for more than one radium treatment postoperatively. I shall

report in detail 3 representative cases which have been under my observation every two or three months for three years. In general, nasal obstruction is the complaint of all these patients; nasal discharge is usually associated. Many have had a large number of operations for removal of polyps, and examination of their noses shows that most of the membrane is involved in polypoid change.

REPORT OF CASES

CASE I (A106551). Female, aged forty years. First came to the Mayo Clinic in 1914 complaining of nasal obstruction of nine years' duration and loss of the sense of smell. Her first operation for the removal of nasal polyps had been performed in 1909. Since then she had had eight such operations.

Innumerable irrigations of both antrums were given without relief and submucous resection of the nasal septum was performed. Not being benefited by this treatment, she left the Clinic.

In 1921, the patient returned to see if any new treatment had been found that would offer even temporary relief. Severe attacks of asthma, which had occurred since the onset of her trouble, had become more frequent during the last two years. The sense of smell was completely lost. We advised our usual operative treatment and radium postoperatively.

On March 5, 1921, a specimen of a polyp was removed from the patient's nose; pathological examination revealed adenomyxoma. All polypoid tissue in the nose was then removed radically and the antrum and posterior ethmoid sinuses, which showed hyperplastic suppurative change, were exenterated. Considerable reaction followed this extensive operation and use of radium was impossible until March 11, when 200 mgm. hours of radiation was applied in each middle meatus. March 21, 200 mgm. hours was applied to each side. Further local treatment, chiefly shrinkage and suction of each middle meatus, was given and the patient was dismissed to return again in two weeks.

On April 9th, when the patient returned, she was most elated over the fact that she was able to smell all odors; from then on her sense of smell was very acute. Two hundred and fifty mgm. hours of radiation was applied in each side of the nose.

On June 2d, the patient again returned, at which time she received 250 mgm. hours of radiation in each middle meatus.

This patient has been seen at least every two months since operation and her nasal condition has remained most satisfactory. In March, 1922, at the time of her last visit, her sense of smell was very acute. She did not have nasal obstruction or discharge, and the region of her nose from which polyps had been removed so many times was now covered by pale membrane resembling fibrous tissue, which was resistant to the probe. There were no polyps in either side.

In this case the effect of the radical operation, followed by 1,800 mgm. hours of radiation, was first, restoration of the sense of smell, lost since 1913; second, elimination of the large number of adenomyxomatous polyps; third, reduction to a minimum of the discharge which had previously occurred from both sides of the nose; fourth, absence of nasal obstruction which had been present for many years.

CASE II (A45999). Female, aged fifty years. First came to the Clinic in 1907 because of severe asthma and nasal obstruction. Between 1907 and 1919, she had frequent attacks of asthma which were so severe that she had become unconscious and hypodermic injections of epinephrin had not given relief.

In 1919, the patient returned seeking relief from nasal obstruction. She had had ten or twelve operations on her nose for removal of nasal polyps—so many, in fact, that she could not remember the number. She had recently had a severe attack of asthma. Multiple myxomatous polyps filled both sides of the nose, and there was associated anterior hyperplastic ethmoiditis. Two operations, one on each side of her nose, were necessary at this time in order completely to remove the polypoid tissue and thoroughly to exenterate the anterior ethmoid labyrinth. On November 20th, 200 mgm. hours of radiation was applied on each side of her nose.

During the following two months the patient was seen every week and then every two weeks until May 20, 1920, at which time 200 mgm. hours of radiation was again applied on each side of her nose. Since then she has been observed at frequent intervals. She has had remarkable relief. Since her operations in 1919 and subsequent radium treatment, she has not had asthmatic attacks. At her last visit, April 1, 1922, there was no nasal obstruction and only a small amount of mucus on the floor on each side of the nose. The middle meatus was free from polyps and the membrane was pale and definitely resistant to the probe.

Case III (A135740). Male, aged forty years. First came to the Clinic in 1915 because of nasal obstruction. Small polyps were found, but apparently the chief cause of obstruction was a fractured septum. A submucous resection of the septum was performed.

The patient returned to the Clinic in April, 1920, because of marked nasal obstruction and discharge. Examination revealed multiple, large, obstructing polyps in both sides of the nose, and hyperplastic suppurative ethmoiditis. The tonsils, which were definitely septic, were removed on April 27th.

On October 21st, the patient returned and the polyps from both sides of the nose were completely removed and radical exenteration of both anterior and posterior ethmoids on each side was performed. Both middle turbinates were involved in the polypoid change and were amputated. A second operation for removal of the polyps was performed on December 3rd. Between this time and February 4, 1921, 1,600 mgm. hours of radiation was applied to the diseased area.

The patient has been seen at intervals of one month; in March, 1922, his nose was still in good condition. There was a slight polypoid change in the posterior end of each middle meatus, which, however, had not progressed. Microscopic examination revealed adenomyoxma.

Many of the other patients in the series of 55 pursued the same course, but it was not possible to observe them frequently after the operations and the treatments by radium.

CONCLUSIONS

Definite conclusions with regard to the results obtained by the use of radium following operation for nasal polyps await more experience and more general use of radium. Information obtained from the observation of cases in this series indicates points as follows:

1. The application of radium should be started on the second or third day after operation.
2. Radium should be applied not oftener than once a week.
3. Two hundred milligram hours of radiation at weekly intervals has not produced a burn, and is, therefore, safe radiation.
4. Radium, in the majority of cases, undoubtedly definitely lengthens the intervals of recurrence.
5. Definite operative cures occur more often with radium than without it.
6. Radium does not affect an associated suppurative sinus disease.

DISCUSSION

Dr. Lillie. The number of recurrences in this type of case following radium treatment has been greatly decreased. It seems to us that radium offers the best chance for the control of this type of disease process in the nose. As our knowledge and experience grow clinically, in the choice of case, and in the choice of the proper dosage to affect the desired change pathologically, it is felt that the management of these cases will be more rational and scientific, and results will be better from the patient's standpoint.

RADIUM TREATMENT OF DISEASED TONSILS*

BY CARL F. ROBINSON, M.D.

BARRE, VERMONT

GRANTED that the tonsil needs treatment whether from infection or hypertrophy, five methods of attack present themselves, namely, (1) the application of radium tubes or needles directly against the tonsil, (2) the application of radium externally over the tonsil, (3) the application of the placque directly, (4) the introduction of radium needles, (5) emanation tubes introduced directly into the substance of the organ.

I will report a series of 75 cases of enlarged and diseased tonsils, treated by radiation, many of which were referred by throat men. Operation was contraindicated because of stone-cutter's disease, heart conditions, hemophilia or fear. The general practitioner, the throat man and myself have been impressed by the manner in which these throats cleared up after radiation.

MODE OF ACTION

According to Witherbee, after *x*-ray treatment of the tonsil, there is an atrophy of the tonsil and an absorption of the immature lymphatic cells in the follicle which lessens the depth, and results in a distortion of the crypt causing an eversion and an evacuation of the crypt contents. Radium probably acts similarly.

We were able to secure good results with the *x*-rays, but on account of the time needed (six to eight treatments two weeks apart), fear of a noisy apparatus, and possible danger to overlying structures, our attention was turned to the possibilities of a direct application of radioactive material.

METHOD OF APPLICATIONS AND TECHNIQUE

Method 1. The tonsil and nasopharynx are swabbed with a solution of novocaine to eliminate gagging rather than to ease pain. Many do not receive this preparatory treatment. Two 12.5 mgm. radium needles are threaded and introduced into the center of the tonsil and left in place from two to four hours. We usually treat both tonsils at the same sitting. The patient rarely has a noticeable reaction from this amount of radiation. In four to six weeks complete atrophy will be found—the anterior pillar having to be retracted in order to find any remaining tonsil.

Method 2. Fifty mgm. of the element—I use four 12.5 needles,—screened by 0.4 mm. steel, 1 mm. brass and one thickness of rubber tubing, is held directly against the tonsil for one hour, by means of the Cameron Adjustable Radium Applicator.

Method 3. A 50 mgm. tube screened with .4 silver, 1 mm. brass and 1 mm. rubber and one-half inch of gauze is applied externally over the tonsil for six to ten hours depending upon the age and skin of the patient.

Method 4. An unscreened 20 or 30 mgm. placque is held directly against the tonsil for one or two hours.

Method 5. Unfiltered emanation introduced into the tonsillar substance.

I have used only the first three methods and will report the results. My first 30 cases were crudely treated by the external method with a more or less complete atrophy in 25. The cases receiving this method of treatment were usually small children and infants whose mothers positively refused the operation, or in whom some contraindicating condition was present. Their ages ran from eight months to fifteen years. Small children received six hours over each tonsil, and older children up to ten hours. I have rarely seen more than a very slight erythema. These patients breathe better in two weeks and the atrophy is very noticeable in four weeks. The second treatment is rarely needed. My own three-year-old baby was treated in this manner, and I thus had the rare opportunity of watching daily progress of the action of the element. The cases which I count more or less as failures were in patients with thick or fat necks and older or chronic tonsils. Even in these cases where a very noticeable atrophy could not be secured there was a marked smoothing out of the surface of the tonsil and less

* Read at the Seventh Annual Meeting of THE AMERICAN RADIUM SOCIETY, St. Louis, Mo., May 22–23, 1922.

susceptibility to frequent attacks of the so-called colds.

Twenty-five cases have been treated by the needle method. All these have responded beautifully to treatment; and I can confidently say that if the throat men would watch such cases with unbiased minds, the operation would be a thing of the past, resorted to only after failure with radium. The men in my vicinity certainly acknowledge that the results are equal to theirs by operation, and without the danger of an anesthetic, hemorrhage or pulmonary abscess. The only apprehension they express is that the result may not be permanent. I have been doing these cases for only a year, and therefore cannot testify on that point. My patients, however, prefer a radium treatment once a year to going through the operation. I might remark here that 15 cases in the series which I am reporting had had one operation, and 3 had had two tonsillectomies. Repeated tonsillar abscesses brought 3 to me.

Twenty cases have been treated by holding the radium applicator directly against the tonsil. This method secured results similar to the needle method. I feel, however, that the needle method is the method of choice because of the perfect application with radiation attacking the tissues in all directions. A smaller amount of radium is needed—12.5 mgm. in the needle as against 50 mgm. in the method under discussion. We find many patients who rebel against even the introduction of the needles, and in such cases we fall back upon either Method 2, or the external one, Method 3.

C. Augustus Simpson, of Washington, D. C., who because of ill-health could not read his paper, uses a 30 mgm. applicator held directly against the tonsil by means of a long applicator for one hour. He writes, "With this original technique it is perfectly remarkable how quickly the tonsil begins to shrink and show atrophic changes. A mild reaction which turns the part white is to be seen where the radium was held. This slight irritation disappears in two to three days. In one patient with a temperature of 101° F., with exudate in the crypts of the enlarged protruding and inflamed tonsils, with cervical glands in the neck the size of half an orange, associated with malaise and loss of appetite, the picture was changed in one week after a single treatment. The enlarged glands disappeared in three weeks and only a part of the tonsil was to be seen when the anterior pillar was pulled to one side."

AUXILIARY TREATMENT

Simpson uses an *x*-ray treatment externally the same day that radium is used. This seems practical, and I now do likewise, giving a four-minute treatment with spark gap of 7 inches, ma. 5, distance 10 inches, filter 3 mm. aluminum over the region of the tonsil, protecting the surrounding tissues with lead, exposing the area plotted as when taking a picture of the lower molars. The patient lies face downward, head turned to one side with a pillow under the chest to throw the head away from the shoulders.

I will digress from straight radium treatment to quote from Witherbee, who probably was the pioneer in radiation treatment of diseased tonsils. His original *x*-ray method created considerable comment when he issued from the Rockefeller Institute the following: "The *x*-ray method . . . is not only safe and permanent, but will more thoroughly and completely remove this focal infection than any other method yet devised, surgical or otherwise; and furthermore, the contraindications for operation in no way interfere with this procedure."

The fifth method, that of using emanation has not been used by us, and I find no records recording its use.

EFFECT ON MICRO-ORGANISMS

We read that radium is not bactericidal, and herein lies the main criticism of radium treatment of infected tonsils. Bacteria are not directly affected by gamma or *x*-rays, but they may be killed by large amounts of beta or alpha rays. As the alpha rays are absorbed on the surface these may be eliminated from the discussion. The beta rays and the secondary beta rays probably are largely responsible for therapeutic results. I have noticed that an acutely inflamed tonsil reacts much better and

quicker than does the quiet tonsil, probably because of the increased amount of blood with its iron content. I am now doing a series in which we inject the tonsil with a solution of iron before radiation, with the idea of stimulating more secondary beta radiation. I am not ready to report on this at this time.

Whatever the cause of the effect, patients radiated for infected tonsils exhibit marked remissions of symptoms such as neuritis, rheumatism, malaise etc., similar to the effect noticed after tonsillectomy.

POSSIBLE CRITICISM

Dr. Murphy, at the 43rd Annual Congress of the American Laryngological Association, warns us thus: "The region of the neck is one containing numerous important anatomical structures which must be carefully guarded against injury. Inasmuch as a knowledge of the safe and effective use of both *x*-rays and radium is acquired only through highly intelligent study and much experience, it is far better that experiments be carried out by those qualified for the work than that the success of a method of such good promise should be compromised and perhaps discredited through errors due to incomplete understanding of the medium or to faulty technique in its application."

Several surgeons have expressed the same thought to me recently, and I find that the general public also is somewhat afraid of this powerful agent. Radiologists, however, scoff at this fear. I have been unable to learn of any harmful results occurring after correct *x*-ray treatment of adenitis. Boggs writes, "Most laryngologists are referring tuberculous adenitis for radiation as a routine procedure." A review of the literature on this subject does not reveal the report of any case in which the untoward effects of radiation on the thyroid, parathyroid, pituitary or parotid gland has been recorded.

ADVANTAGES OVER OPERATION

These are obvious—no anesthetic, no danger of hemorrhage, lung abscess, damaged pillars, etc., no loss of time, and equal results. In a few instances it has been noted that the ear condition, chronic catarrhal otitis media, when present, has been benefited. This subject requires, it would seem, more extended observation, and opens up a field pregnant with possibilities.

ADVANTAGES OVER *X*-RAY TREATMENT

There is no danger, in the direct methods, of causing a disfiguring burn, and if there is danger to overlying structures by *x*-radiation, direct radium application eliminates this objection. In children and nervous adults the simple radium applicator arouses no fear, whereas the *x*-ray apparatus may frighten the timid.

CONCLUSION

Radium seems to me to be the agent of choice, no matter what method is under discussion. It requires but one application, and it can be relied upon to do the same thing under the same circumstances—something that the surgeon and the *x*-ray technician cannot always do. The introduction of the needle directly into the substance of the tonsil, supplemented, if desired, with the external *x*-ray treatment, seems to be the most logical of the different methods of radium application.

DISCUSSION

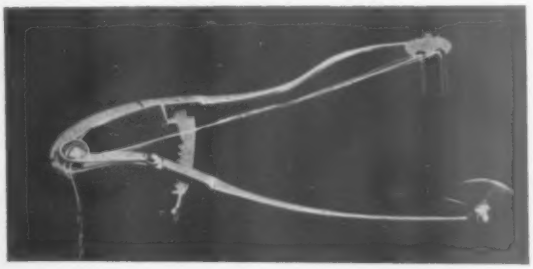
DR. WITHERS. I do not like to take up time for the discussion of so small a point as the treatment of tonsils by radium, except to call attention to the fact that Dr. Robinson has not mentioned the use of bare tubes of radium emanation in the treatment of so-called hyperplasia of the tonsil and lymphatic tissue of the pharynx.

The use of such bare tubes is, to my mind, the treatment of choice, and I can speak from personal experience in regard to this mode of application, inasmuch as there were embedded into my tonsils two weeks ago two small spicules, each containing 0.4 mc. of emanation. This method has been tried out on a small series of cases, and a report was given in *The Laryngoscope* for March, 1922.

After having used surface applications by means of radium plaques, and interstitial applications by means of needles, I am convinced that the use of bare tubes of emanation, two or more of such tubes, containing about 0.2 mc. of emanation, embedded in each tonsil, is the method of choice. It is frequently unnecessary to use even a local anaesthetic for the introduction of these bare tubes. The reaction

is not painful and is confined to the depths of the tonsil, which does not interfere with swallowing, so that patients are more comfortable, during the radium reaction, than with the use of either needles or plaques.

DR. BROEMAN. I have not personally treated a sufficient number of hypertrophied



tonsils with radium to report on its efficacy in this condition. I would however, like to show a simple applicator for the surface treatment of enlarged tonsils that I have found to work very satisfactorily.

I have taken the ordinary Corwin and Wilder tonsillar hemostat which has been on the market for years, and had the ball end removed. This ball end as a rule, is placed in the cavity after the tonsil has been enucleated to control the bleeding. In place of this end I had a small brass plate made to hold two of the universal silver 25 mgm. radium tubes. The tubes are retained in the grooves by means of small wire clamps. Silk thread can be passed through the ends of the silver tubes if desired as another safeguard against losing the tubes. A small piece of rubber dam is placed over the entire end. The cost of this applicator is about $12.00. My main reason for showing it is its simplicity and inexpensiveness. Anyone who has radium tubes can use it without purchasing a special radium tonsillar applicator, which has a limited field of use.

DR. PFAHLER. I will simply say that I used this apparatus in the treatment of my own tonsils, which shows my faith in it, and I also treated my wife's tonsils in the same way, which shows still more faith.

CARCINOMA OF THE ANTRUM*

BY D. CROSBY GREENE, M.D.

Report of Treatment by Radium: Technique and Statistics. From the Clinic of the Huntington Memorial Hospital

BOSTON, MASSACHUSETTS

IN dealing with the treatment of carcinoma of the antrum by radium, we are at once confronted with difficulties, due, in the first place, to the lack of definite knowledge in a given case as to the extent of invasion of adjacent and deeper structures, and in the second place, to the inaccessibility of the deeper parts of the growth to effective radiation.

As to the first difficulty, anterior and posterior rhinoscopy and the *x*-ray give some assistance in locating the direction and extent of the growth, but this is, at best, indefinite and uncertain, as may be often demonstrated when the full extent of invasion is exposed at operation. As to the difficulty of inaccessibility, I believe this can only be overcome by an open operation which will give a wide permanent access to all the nasal and paranasal cavities.

Cases of carcinoma of the antrum may be divided into two groups:

1. Those originating in the antrum or adjoining nasal or paranasal cavities.

2. Those which originate in the epithelial structures of the mouth or the teeth. In both groups, as the disease progresses, we may find it disintegrating the bony barrier which separates the mouth from the antrum, and breaking through, in one type, from the mouth into the antrum, and in the other, advancing from the antrum into the mouth or the soft structures of the cheek.

The tendency for the growth, starting in the antrum, to invade the postethmoidal and sphenoidal sinuses is quite characteristic. Sometimes we find it breaking through the nasal septum and invading the sinuses of the other side. These cases are not suitable for surgery alone, but the combined treatment by surgery and radium has been productive of a considerable proportion of favorable results. In using

*Read at the Seventh Annual Meeting of THE AMERICAN RADIUM SOCIETY, St. Louis, Mo., May 22–23, 1922.

this method we assume that the operative part of our treatment alone is incomplete. That is, although we remove all visible tumor, it is usually impossible to go sufficiently wide of the limits of the growth in the cases as we see them, to avoid leaving some cells in the periphery which will go on to proliferate. The result of the operation is to bring the region involved within the field of radiation, and keep it under observation for an indefinite period. A wide permanent opening is left for this purpose. This opening is made, in the cases originating in the antrum, through the cheek; in those starting in the buccal cavity, the approach may be through the mouth. In our experience the procedure of choice in these cases consists in a wide exposure and removal of the growth followed by radiation of the resulting cavity.

In this report I propose, first, to give a brief summary of the results to date of 84 cases of carcinoma of the antrum admitted to the Huntington Hospital during the six-year period, 1916 to 1921. These cases are divided into 4 groups:

1. Those in which no treatment was attempted, either on account of the hopeless condition of the patient, or on account of refusal of treatment by the patient (6 cases).

2. Those which were operated upon without subsequent radiation (8 cases).

3. Cases treated by radium alone, including cases of recurrence after operation elsewhere (33 cases).

4. Cases treated by radium immediately, or shortly after operation (36 cases).

END RESULTS TO DATE

Group 1. No treatment; (6 cases).
- Died....4
- Untraced....2

Group 2. Operation, no radiation; (8 cases).
- Recurrence (died 5, untraced 2)....7
- Well, 3 years after operation....1

Group 3. Cases treated by radium alone; (33 cases).
- Died from the disease....24
- Treated without permanent improvement, *untraced*.... 7
- Alive and under treatment, but growing worse.... 1
- Apparently well 2½ years after beginning treatment.... 1

Group 4. Cases treated by radium immediately or shortly after operation; (36 cases).
- Died from recurrence.... 11
- Died from hemorrhage, secondary to operation.... 1
- Died from metastases without local recurrence.... 3
- Died from meningitis, secondary to operation.... 3
- Died from other disease, without recurrence.... 1
- Alive with recurrence and under treatment.... 3
- Alive without evident recurrence.. 12
- Untraced.... 2

A comparison of these groups shows that by far the most favorable results have followed the method of operation followed by radiation. This is the method we advocate except in hopeless cases in which only palliative treatment is indicated.

Of the 12 cases in this group, living without recurrence, the time elapsed since operation is as follows:

1 case.....	5 years	1 case.....	2 years
3 cases....	3½ years	3 cases....	1½ years
2 cases....	3 years	2 cases....	1 year

Only 6 of these cases have passed the three-year limit and can be considered as probably cured. The percentage of these is 16⅔, while the percentage of cases free from recurrence for one or more years is 33.

The operation preliminary to radiation is an essential part of the technique.

Operation. The surgical approach employed is through that portion of the face or mouth which gives best access to the tumor in the individual case. In the majority of cases in our series, the incision has been through the face because in these cases the antrum and acessory sinuses were chiefly involved. A modified Moure incision extended horizontally outward to about the center of the malar prominence and vertically upward to the inner portion of the eyebrow, is the one which we have most frequently used.

The soft tissues and periosteum are elevated from the anterior and external wall of the nose on the affected side. Frequently in the course of this procedure, a portion of the growth is encountered which

has destroyed and penetrated the wall of the antrum. The entire bone surface uncovered, is removed by chisel and rongeur. This gives a large opening and good access to the growth, which is now rapidly curetted out. Extension of the growth into the nose and other sinuses is followed up by removal of the entire nasoantral wall and complete exenteration of the ethmoid and sphenoid sinuses. The inner part of the floor of the orbit, the lachrymal bone and orbital plate of the ethmoid, may also have to be removed. Extension of the disease into the oral cavity may necessitate excision of a considerable portion of the alveolar process and hard palate also. The large cavity thus left is carefully examined with a view to the removal of any remains of tumor tissue. When this has apparently been satisfactorily accomplished and the bleeding controlled, the flap of skin overlying the anterior surface of the antrum is cut off at its base, leaving a wide, triangular opening for subsequent observation and treatment.

The actual removal of the tumor is accompanied by rather profuse hemorrhage, which, however, usually stops in a rather surprising manner after the growth has been curetted out. Occasionally, bleeding persists, but it can be dealt with effectively by ligature or pressure, on account of the easy access afforded by the large facial opening.

Steel-jacketed radium tubes, covered with rubber tubing, are now applied to the periphery of the cavity, being distributed over the surface and held in place by gauze packing, soaked in sterile alboline. The dosage employed varies from 500 to 1,000 mc. hours. I wish to emphasize the importance of the application of the radium tubes by the operator himself. It is essential that one who is thoroughly acquainted with the topography of the field, who knows in what regions the growth may not have been most thoroughly removed, and who is equipped to see the remoter parts, and place the tubes accurately, should make the application.

When the growth presents itself most prominently in the mouth, the best method of approach is, I think, from this direction. The incision is made well outside the periphery of the tumor, as it appears on the hard palate and alveolus, and a large opening made into the antral cavity through which the tumor is removed by curettes and rongeurs, and its extensions beyond the antrum followed up and removed. This method of approach is advocated by New of Rochester, who performs his entire operation with the cautery. It does not give nearly as good access to the posterior ethmoid and sphenoid regions as the opening through the cheek. The exact method of approach is not, however, the essential thing. A wide opening, giving free access to the affected region, and thorough removal of all visible tumor, followed immediately by strong radiation of the cavity, are I think, the important factors in the treatment.

After the first radiation the patient is kept under close observation, and any area in which there is a suggestion of beginning recurrence, is subjected to further radiation.

ABSTRACT OF CASES TREATED BY OPERATION FOLLOWED BY RADIATION

Case I. Hospital No. 15.42.27. Male, aged fifty-one. Examination, extensive recurrent tumor of upper jaw, antrum and nose with large buccal opening. Operation, curettage of antral cavity through mouth, followed by radium treatment. Microscopical examination, carcinoma, J. H. Wright. Result, this patient lived at a distance and did not report personally. Reported by mail one year after operation, as being well.

Case II. Hospital No. 16.259. Female. Examination, tumor of upper jaw, antrum and ethmoid. Operation, facial route. Exenteration of tumor. Radium treatment begun on sixth day after operation. Five treatments. Microscopical examination, reported from Massachusetts General Hospital, carcinoma, H. F. Hartwell. Result, recurrence. Died in one year and four months.

Case III. Hospital No. 16.75. Male, aged sixty-one. Examination, recurrent tumor of antrum. Operation, facial route. Excision of tumor involving antrum and ethmoid followed by radium treatment.

Microscopical examination, carcinoma, reported from Massachusetts General Hospital. Result, four years after operation, no local recurrence. Died four and one-half years after operation from lesion in liver, probably metastasis. No autopsy.

Case IV. Hospital No. 17.320. Female. Examination, large opening, right side, roof of mouth, leading into antrum, result of operation by Dr. Finney at Baltimore two months before, which was followed by radiation, 500 mc. one hour. Second prophylactic radiation at Huntington Hospital, 260 mc. two hours. Microscopical examination, reported from Johns Hopkins Hospital, squamous cell carcinoma. Result, no recurrence five years after operation.

Case V. Hospital No. 17.500. Female, aged forty-six. Examination, extensive, recurrent tumor, involving right antrum and roof of mouth. Operation, facial route. Excision of tumor from antrum, ethmoid and sphenoid, followed by radiation. Microscopical examination, reported from Massachusetts General Hospital, H. F. Hartwell, carcinoma. Result, well three years after operation.

Case VI. Hospital No. 17.615.275. Female, aged thirty-four. Examination, extensive tumor, upper jaw and antrum. Operation, facial route. Excision of tumor followed by radiation. Microscopic examination, not recorded. Result, death from recurrence one year and two months after operation.

Case VII. Hospital No. 18.74. Male, aged forty-two. Examination, wide opening right side, roof of mouth, leading into antrum—the result of operation at Boston City Hospital, Dr. J. B. Blake, one year previous. Recurrent tumor in walls of antral cavity. Operation, curettage, followed by radiation. Microscopical examination, carcinoma, J. H. Wright. Result, died from recurrence one year and two months after operation.

Case VIII. Hospital No. 18.332. Male, aged fifty-one. Examination, wide opening from mouth into antrum from operation at Boston City Hospital, ten days previous. Three radium treatments, each about 30 mc. hours. Microscopical examination, reported from Boston City Hospital, carcinoma. Result, death from pneumonia, four months after operation. Autopsy report, Boston City Hospital, no evidence of carcinoma, bronchopneumonia.

Case IX. Hospital No. 18.653.277. Female, aged fifty-two. Examination, tumor of left cheek, left exophthalmos. Operation, facial route. Excision of tumor, followed by radiation. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence. Died two years after operation.

Case X. Hospital No. 18.775. Male, aged sixty-three. Examination, tumor of right cheek, ulceration of overlying skin, cheek and nose. Operation, facial route. Excision of tumor, followed by radiation, 1012 mc. hours. Second radium treatment, one month later, 900 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, well three and one-half years after operation.

Case XI. Hospital No. 19.16. Male, aged fifty. Examination, tumor, completely blocking left nostril. Operation, facial route. Excision of tumor. Five radium treatments, beginning four days after operation, 75 mc. hours. Three days later, 140 mc. hours. One month later, 64 mc. hours. Two weeks later, 54 mc. hours. One month later, 46 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, well two and one-half years after operation.

Case XII. Hospital No. 19.101. Male, aged thirty-six. Examination, tumor mass obstructing left nostril. Operation, facial route. Excision of tumor, followed by one radium treatment, 75 mc. hours. Microscopical examination, malignant adenoma, J. H. Wright. Result, well three and one-half years after operation.

Case XIII. Hospital No. 19.109. Male, aged seventy-three. Examination, operative opening in mouth leading into left antral cavity. Tumor mass involving greater part hard palate on right side. Polypoid masses, occluding both nares. Operation, curettage of tumor through mouth, followed by radium treatment beginning one week after operation. Twenty-two radium treatments. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence from time to

time, apparently controlled by radiation. Alive with recurrence at present, three years after operation.

Case XIV. Hospital No. 19.170. Male, aged fifty-six. Operation, facial route. Excision of tumor involving antrum, ethmoid, sphenoid and septum. Microscopical examination, carcinoma, J. H. Wright. Result, died from meningitis, three days after operation.

Case XV. Hospital No. 19.757.346. Male, aged fifty-six. Examination, tumor of left cheek. Operation, facial route. Excision of tumor involving antrum and ethmoid. Microscopical examination, epidermoid carcinoma, J. H. Wright. Result, recurring, secondary hemorrhages from which he died four months after operation.

Case XVI. Hospital No. 19.363. Male, aged fifty-seven. Examination, wide opening, left side, roof of mouth, leading to cavity of antrum and left nostril, result of operation two months previous at Manhattan Eye and Ear Infirmary. Recurrence of growth noted in posterior and upper parts of cavity. Radium treatment, seed insertions into tumor masses on three occasions, first, 2 seeds, each 4 mc.; second, two weeks later, 1 seed, 4 mc.; third, three months later, 1 seed, 4 mc. Microscopical examination, reported from Manhattan Eye and Ear Infirmary, carcinoma. Result, patient reported by mail three years later, well.

Case XVII. Hospital No. 20.150. Male, aged fifty-nine. Examination, tumor, right upper jaw and antrum. Operation, partial excision of right upper jaw through mouth. Curettage of tumor, followed by radium treatment, 402 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, rapid recurrence. Died two months after operation.

Case XVIII. Hospital No. 30.203. Male, aged seventy. Examination, tumor of left antrum. Operation, facial route. Five radium treatments beginning one month after operation. Microscopical examination, reported from Massachusetts Eye and Ear Infirmary, carcinoma, Dr. Verhoeff. Result, died from recurrence eleven months after operation.

Case XIX. Hospital No. 20.233. Male, aged forty-five. Examination, tumor obstructing right nostril. Operation, canine fossa route. Excision of tumor followed by radium treatment through the nostril. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence after one and one-half years, patient alive and under treatment.

Case XX. Hospital No. 20.389. Female, aged thirty-eight. Examination, tumor involving right antrum. Operation, facial route. Excision of tumor. Radium treatments begun three weeks later, three treatments. Microscopical examination, report from Massachusetts Eye and Ear Infirmary, carcinoma, Dr. Verhoeff. Result, died six months after operation.

Case XXI. Hospital No. 20.433. Male, aged fifty-three. Examination, tumor, left upper jaw and left side of nose. Operation, buccal route. Excision of tumor followed by radium treatment. Microscopical examination, carcinoma cells, resembling histologically, the enamel organ—adamantinoma, J. H. Wright. Result, well two years after operation.

Case XXII. Hospital No. 20.559. Male, aged fifty-one. Examination, tumor of left antrum involving left nostril. Operation, facial route. Excision of tumor from left antrum and ethmoid, followed by radium treatment, 140 mc. hours. Microscopical examination, reported from Massachusetts Eye and Ear Infirmary, carcinoma, Dr. Verhoeff. Result, no recurrence two years after operation.

Case XXIII. Hospital No. 20.894. Male, aged fifty-three. Examination, tumor of right antrum. Operation, buccal route. Excision of tumor, followed by radium treatment. Microscopical examination, squamous cell, carcinoma, J. H. Wright. Result, died from recurrence six months after operation.

Case XXIV. Hospital No. 20.190. Male, aged sixty-seven. Examination, small opening in cheek, result of operation six days previous at Massachusetts Eye and Ear Infirmary. Radium applications within cavity of antrum beginning six days after operation. Microscopical examination, reported from Massachusetts Eye and Ear Infirmary, carcinoma, Dr. Verhoeff. Result, died from recurrence ten months after operation.

Case XXV. Hospital No. 20.1511. Female, aged forty-six. Examination, tumor of left cheek and antrum. Operation, buccal route. Excision of tumor, followed by radium treatment, 260 mc. hours. Two subsequent treatments. Microscopical examination, epidermoid carcinoma, J. H. Wright. Result, not known, untraced.

Case XXVI. Hospital No. 20.1166. Female, aged fifty-nine. Examination, tumor of right antrum, occlusion of right nostril by tumor. Operation, facial route. Excision of tumor, followed by radium treatment, 450 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence noted six months after operation which was treated by radiation and later, further operation. Enucleation of right eye, eleven months after first operation. Alive one and one-half years after first operation, six months after second operation. Recurrence now.

Case XXVII. Hospital No. 20.1282. Female, aged forty-one. Examination, wide opening in left cheek, communicating with cavity including antrum, ethmoid and sphenoid sinuses, result of operation two weeks previous at Eye and Ear Infirmary. Tumor had involved chiefly ethmoid and sphenoid. Radium treatment, 164 mc. hours. Second treatment two weeks later, 104 mc. hours. Microscopical examination, reported from Massachusetts Eye and Ear Infirmary, carcinoma, Dr. Verhoeff. Result, died six months after operation. Autopsy showed no local reccurence. Metastases in abdomen.

Case XXVIII. Hospital No. 20.1177. Female, aged fifty-seven. Examination, tumor, right antrum. Right nostril completely blocked by tumor. Operation, facial route. Excision of tumor, followed by radium treatment, 747 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, patient well one and one-half years after operation.

Case XXIX. Hospital No. 21.216. Male, aged thirty-eight. Examination, recurrent tumor of antrum. Operation, at Massachusetts Eye and Ear Infirmary, facial route. Excision of tumor, exenteration of antrum, ethmoid and sphenoid, followed by radium treatment, Dr. H. P. Mosher. Microscopical examination, reported from Eye and Ear Infirmary, adenocarcinoma, Dr. Verhoeff. Result, reported by Dr. Mosher as free from recurrence one and one-half years after operation.

Case XXX. Hospital No. 31.219. Female, aged sixty-three. Examination, tumor of left cheek. Growth obstructing left nostril. Secondary operation, facial route. Excision of tumor, followed by radium treatment, 57 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence. Died six months after operation.

Case XXXI. Hospital No. 20.212. Male, aged forty-seven. Examination, recurrent tumor of right upper jaw, extending into antrum. Large opening leading from mouth into antrum cavity. Operation, buccal route. Curettage of cavity, followed by radiation. Microscopical examination, carcinoma, J. H. Wright. Result, unknown, patient lost sight of.

Case XXXII. Hospital No. 20.558. Female, aged fifty-four. Data incompletely recorded. Operation, facial route. Excision of tumor, followed by radiation, four weeks after operation. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence, untraced.

Case XXXIII. Hospital No. 21.839. Female, aged forty-seven. Examination, tumor of antrum, right. Obstruction of right nostril by growth. Operation, facial route. Excision of tumor, followed by radium treatment, 2430 mc. hours. Microscopical examination, carcinoma, J. H. Wright. Result, recurrence. Death in five months.

Case XXXIV. Hospital No. 21.1160. Male, aged forty-one. Examination, tumor, right antrum and upper jaw. Operation, facial route. Excision of tumor, followed by radium treatment. Microscopical examination, carcinoma, J. H. Wright. Result, died of meningitis on sixth day after operation.

Case XXXV. Hospital No. 15.4227. Male, aged fifty-one. Examination, large opening, left side, roof of mouth, communicating with antral and nasal cavities, the result of ulcerations from treatment by liquid air. Recurrence of tumor in left antrum. Operation, buccal route.

Curettage of tumor, followed by radium treatment. Microscopical examination, carcinoma, J. H. Wright. Result, patient alive and doing well, one year after operation.

CASE XXXVI. Hospital No. 20.1325. Male, aged fifty-two. Examination, ulcerating tumor of left upper jaw extending into antrum. Operation, buccal route. Excision of tumor followed by radium treatment, 1776 mc. hours. Patient well one and one-half years after operation.

DISCUSSION

DR. PANCOAST. I heard Dr. Greene read a paper on this subject about a year ago and was very much attracted by the technique which he employs because of the easy access it gives to the antrum and other sinus for the application of radium primarily, and particularly during subsequent treatment. I think that is a very important part of any technique. The large opening also permits watching for any recurrence through the months or years that follow. I have observed a case several times that was operated on by Dr. Greene and was much surprised at the ease with which one could watch the area in this way. It is very much better than through an opening made in the mouth in which one has a great deal of difficulty in watching for recurrences as well as in making the application.

DR. CLARK. I have been called upon to treat a great many cases of malignant disease of the antrum, both primary, and recurrent after operation. I have attacked this lesion by the electro-coagulation method through an opening similar to the one described by Dr. Greene. Where there has been post-orbital involvement, and a complete exenteration is found necessary at the same time, I prefer an opening through the floor of the orbit. I have also treated the antrum by way of the canine fossa, but my best results have been obtained by entrance through the hard palate and alveolus. A mouth-gag is employed and a transverse suture drawn through the tongue, which may then be pulled forward out of the way. It may be necessary also to use a tongue-depressor. A long sharp needle is used as the active electrode. The soft tissue and bone are quickly devitalized by the current and immediately removed with bone instruments without hemorrhage. The contents of the antrum are also coagulated and curetted away, likewise without hemorrhage. Radium may then be used, but care should be taken not to overtreat, else it will be found that necrosis of the bone will result, which is in itself a serious matter. Heavy radium or *x*-ray treatment should, however, be employed in addition from the outside. Experience has taught that even advanced sarcomata and carcinomata of the antrum can be thus treated with considerable hope of success. Very satisfactory dental plates can subsequently be made, which will permit of the patient talking plainly and also prevent food from collecting in the antrum.

DR. BLOODGOOD. I believe this treatment of tumors of the antrum, nasal cavity and other sinuses offers a great opportunity. I have in my laboratory the records and specimens of an accumulated material of thirty years. We have gone over this again and again, and when we come to estimate what the operation for the removal of the upper jaw has accomplished, no matter how extensive, or the removal of growths within the nose, or the curetting of sinuses accessory to the nose with a knife or curette, we find we have not a single cure in all those years of undoubted carcinoma or sarcoma. Now, if we would include certain cases in which the radical operation has been done, we would have a great many cures, but they are not carcinoma and not sarcoma. So surgery alone in the antrum, nasal cavity and other sinuses, has nothing to offer. The next point is that of diagnosis. You can divide all this accumulated material into three groups: In one there will be no disagreement that all the cases are cancer or sarcoma. In this group there are no cures. In the next group there is no question as to the diagnosis that they are all benign. In this group there are not many radical operations. There were a few resections of the upper jaw for cysts and giant cell tumor that were not necessary. Then there is the third or border-line group, largely diagnosed sarcoma, and to that group I think belong the cases shown here microscopically—the fibromatous and myxomatous tumors. Most of these are well after a radical operation; apparently the radical operation was not necessary. That leads to a very important conclusion. If you have a tumor of the antrum or nasal cavity or other sinuses, you have no evidence that a mutilating operation with the knife will accomplish a cure. If you take pieces out for diagnosis, you know you are dealing in some instances with malignancy, and in some with benignity; also without any doubt, in a very large group you do not know what you are dealing with. Therefore, as we cannot diagnose positively the border-line group, and cannot cure by surgery the malignant group, what can we do for these two groups?

My first change was from the knife to the cautery and I have now one five-year cure of a cancer of the antrum in which I opened the antrum and burned out the tumor with a cautery, and later removed the glands of the neck which were metastatic. This patient is well over five years, and that is my only case. I have three cases of fibromas, well after five years, treated by cautery. These may or may not be sarcoma.

What I wish to urge is a careful study of these tumors and the application of the things that are valuable today, such as radium and *x*-ray, the direct attack of the local growth, and perhaps in the sinuses, where you can have a large opening, the ordinary electric needle. It seems to me a large number of cases of malignant disease of the sinus might be treated by means of electrocoagulation necrosis. I think if Dr. Pfahler and Dr. Clark will invite me to Philadelphia, I would like to study this method of destruction of tissue by the cautery, the only one which can be applicable for the same opening in nasal and sinus diseases. I do not know what the danger is of incomplete removal of tissues, in which radium and *x*-ray follow and precede that method, but my whole experience shows that if a malignant disease is cut into by a knife or a curette you might as well send for the undertaker. It disseminates the disease. The same is true of some of the benign tumors, such as myoma. Some say these always recur. I have recently reported that without exception every myoma cut into in my entire experience has recurred. Of course, a chondroma or a lipoma cut into and removed, may not recur. Those of you working in connection with nose and throat men have a very great opportunity. I think you will begin to feel that malignant disease of the sinuses is much more common than you think. In my experience, the treatment by surgery alone has been hopeless.

Dr. Stone. The technique of treating these tumors is one which the late Dr. Janeway initiated and carried out, in many instances, to a successful conclusion. It appeared at first to be an unsurgical method, and I did not think it would be successful. Dr. Janeway learned that in order to attack the tumor successfully by means of radium a sufficiently large opening must be made. In the first few cases the necrosis was so severe and was allowed to remain so long that the pain and suffering did not appear to justify the effort. Finally, however, he learned that by curetting carefully the necrotic areas, the pain disappeared. If any tumor tissue remained, the imbedding of the emanation and the curetting of the necrotic tissue were repeated, so that success crowned his efforts in numerous instances. It requires painstaking effort, but I believe that cases have been cured in this way which could not have been cured by any other procedure.

Dr. Burnam. I have been interested in this subject for a long time. It should be remembered that many of the tumors of the antrum are sarcomas; they are perhaps not as common as carcinomas, but they are common enough. Many of these sarcomas can be cured by heavy external radiation without opening the antrum and without any operation. No squamous cell carcinoma can be cured in this way. We have had a great many malignant tumors of the antrum. The sarcomas are treated either by external radiation alone or by a combination of external and internal radiation. The carcinomas have been treated by operative removal and radiation and by simple exploration and making a way for radiation treatment intra-antral. One of these carcinoma cases was operated on by Dr. John Finney in 1913. He explored from the front of the face very much in the way that Dr. Greene has been doing. There was a great opening into the antrum with a definite recurrence on the posterior wall. This patient was treated by local tubes, he remained well for a number of years and the defect in the face was finally closed by a plastic operation. Another patient of six years ago came to Dr. Finney after seeing surgeons in Boston, New York and Philadelphia. She had, not an early carcinoma, but one still limited to the antrum. The *x*-ray pictures showed clouding of the entire antrum. The late Dr. Janeway had seen her and expressed an opinion that it was an entirely hopeless case from the operative standpoint. Dr. Finney sent the patient to me for an opinion. At that time I had not very definite ideas as to what should be done in these cases, but, after consultation, we decided that the combination of operation and radium was the best treatment. I believe this patient is still well.

Dr. Bloodgood has worked with and helped me in many of my cases. In many of the patients on whom he has operated, there has been an opening through the palate, which allowed an inspection of the antrum and the topical treatment equally as well as the opening through the face. It seems to me, therefore, that the opening through the mouth should be considered in some cases. I do not know whether it is preferable as a routine or not; it is probably easier to close the opening in the face by a plastic than it would be in the mouth.

Dr. New. Dr. Greene emphasizes particularly the classification of these tumors from

the anatomic standpoint and, in this way, has placed them in several groups. We know that a tumor that involves the antrum secondarily is entirely different from a primary tumor of the antrum, with regard to the prognosis. In the tumors involving the jaw primarily and the antrum secondarily, statistics will show a much higher percentage of cures than in the primary antrum growths.

I wish particularly to discuss two points. First, I do not believe that a malignant tumor should be curetted, and, if Dr. Greene would use some form of cautery in removing such tumors, his end-results would be still better. Second, I do not believe it is necessary to open the antrum through the cheek in order to obtain sufficient exposure to remove these tumors thoroughly. The procedure of choice is to explore the antrum above the alveolar process or through the palate, and by the use of water cooled retractors obtain a good exposure, even if the growth invades the nose or ethmoids.

NOTE. Slides were used to show that extensive tumors of the antrum could be removed through the mouth with the cautery, leaving practically no external deformity, the opening in the mouth being closed later by a dental plate.

DR. GREENE (closing discussion). Dr. Bloodgood's criticism may be justified in the report of the cases as I have given them, for I have not given the details of the microscopic findings in each of the cases. I have an abstract of these findings which I have not read. In every case we had a report of carcinoma by a pathologist of standing. Most of the examinations were made by Dr. J. H. Wright of the Massachusetts General Hospital. In view of what Dr. Bloodgood has remarked, however, I feel that in reporting any such series of cases as these it is important that slides should be available for further examination, and I propose sometime in the near future to go over some of these slides with Dr. Bloodgood himself.

As to the method of approach at operation, I feel that where the cribriform plate has been involved, as it has in many of my cases, the approach through the face has a decided advantage over that through the mouth. Many of these cases were hopeless from the surgeon's standpoint, and yet we have had a fair proportion of favorable results.

STATISTICS AND TECHNIQUE IN THE TREATMENT OF MALIGNANT NEOPLASMS OF THE LARYNX*

BY DOUGLAS QUICK, M.B. (TOR.), AND F. M. JOHNSON, M.B. (TOR.)

Attending Surgeon, Memorial Hospital — Adjunct Assistant Surgeon, Memorial Hospital

NEW YORK CITY

IN discussing the use of radium in treating cancer of the larynx, several factors relative to this new physical agent must be considered. Radium is not a cure-all, but it has limited the field of operability to strictly early cases, at least, and in these, if operation for other reasons is contraindicated, with sufficient experience and an adequate supply of radium, it is perfectly justifiable to depend upon this agent alone. Certain types of malignant disease respond very favorably to radium, and in these we feel we are well beyond the experimental stage. In other types, either the resistance of the growth itself or various other factors, have made progress slow. Unfortunately, laryngeal cancer belongs in this group and the present report of our experience at the Memorial Hospital must be looked upon as incomplete experimental evidence rather than a definitely proven method.

We feel, however, that the results to date give definite proof of the value of this agent and warrant the drawing of certain conclusions.

Here, as in other types of malignant disease, the work has been carried out almost entirely on advanced and hopeless cases. This is more especially true of the earlier years of the work. Technique is continually changing as clinical information accumulates, so that in comparable cases the work of today cannot be compared with that of one, two or five years ago. For these reasons, a report for statistical

*Read at the Seventh Annual Meeting of THE AMERICAN RADIUM SOCIETY, St. Louis, Mo., May 22-23, 1922.

purposes at present would be both useless and misleading.

The literature on the subject to the present time gives very little data of value. Reports are invariably of small groups or single cases, are usually incomplete, and deal chiefly with palliative results in advanced cases only.

It is not my purpose here to discuss radium in primary operable cases as compared with the various surgical procedures. While I, personally, offer no apology for treating such cases with radium, I frankly admit that sufficient data is not available on paper to prove the wisdom of such a course.

There are many factors that make us look to radium as a possible advance in the treatment of cancer of the larynx. Leaving out of consideration the so-called operable cases, with all the attendant dangers and disappointments of radical surgery, we still have a vast group in which surgery offers nothing. A considerable percentage of intrinsic growths and—I believe I am correct in stating—practically all extrinsic growths, are inoperable when seen by the laryngeal surgeon. It is from this group, largely, that our radium data must be obtained, for it offers possibilities of more than has heretofore been accomplished.

In applying radium to a laryngeal growth, certain difficulties arise which are not met with in other parts of the body. If efficiently applied, radium creates a sharp inflammatory reaction of several weeks' duration, and in the cases under discussion this reaction is just at the vantage point of two body systems. It often interferes with both swallowing and breathing. Hence the danger of impairment of the patient's general health, which is usually already undermined. It is impossible to put the treated part at rest and consequently the factor of mechanical irritation is added. It is very frequently impossible to determine accurately the extent of disease in these cases. Vision alone is not sufficient aid in satisfactorily examining a malignant growth. Palpation, to determine the depth of neoplastic infiltration, is most important, but, except for a few extrinsic lesions, this is impossible in laryngeal work.

CLASSIFICATION OF CASES

For the proper management of the patient a careful appraisal and classification is one of the first essentials. From a statistical standpoint it is imperative, and it is equally necessary in order to determine the method of and extent to which treatment with radium should be pushed. For statistical purposes, cases must be divided of course into intrinsic or extrinsic, primary or recurrent, and operable or inoperable. For treatment purposes they should be classed as "operable" or "inoperable" to radium. The "operable" group should be further divided as favorable or unfavorable, depending on whether a complete regression or only palliative relief can be reasonably hoped for. The group classed as "inoperable" to radium should be left alone as far as this agent is concerned. There comes a time in the treatment of malignant diseases when even the physical agents are of no avail for palliative relief. Unfortunately, a considerable number of laryngeal carcinomas can be relieved only by opiates and tracheotomy. I am convinced that, in our own service, several patients have been treated who would have been better off had no radium been used.

METHODS OF TREATMENT

Once the decision to use radium has been made, it is essential to decide what can be reasonably hoped for by its use. Treatment designed to eradicate the disease is attended with considerable discomfort for several weeks at least. The inflammatory reaction causes pain, and may interfere with swallowing and breathing as a result of edema. In bulky extrinsic growths, sloughing and hemorrhage must be reckoned with. A tracheotomy may be necessary before beginning treatment or may become imperative later on. If there is any question as to the necessity for tracheotomy, I am convinced it is best to err on the side of safety and do it early. If there is a reasonable chance to produce a complete regression of the disease, it is then perfectly justifiable to push treatment to the limit and risk putting the patient through a strenuous period of discomfort. If, on the other hand, only palliative relief can be

hoped for, then the pateint's physical comfort demands first consideration throughout.

RADICAL TREATMENT BY RADIUM

This is obviously a relative term. We now have a large fund of available information both on the physics of radium and on its action on malignant growths in various parts of the body. Our big problem at present is to apply this information in perfecting our laryngeal technique. The technique of using a scalpel to best advantage has required several generations. Radium must be looked upon as a new instrument with the technique of its application in the making. Too often we see reports of radium applied in the larynx in a manner which signifies utter disregard of available information. We have long since passed the time when a piece of radium could be placed in the vicinity of a new growth and adequate treatment assumed. Accuracy and, to a certain extent, intimacy of application are essential. Each case must be studied individually and a plan of treatment outlined which will give the greatest intensity of radiation in the diseased area with least damage to surrounding normal structures. The only place where anything approaching a stereotyped method is permissible is in the external radiation. I believe that every case accepted for treatment should receive intensive radiation by heavily filtered radium applied over both sides of the neck and directed toward the primary growth. For this we have employed filtration of 2 mm. of brass and doses ranging from 2,200 mc. hrs. at 3 cm. distance to 9,000 mc. hrs. at 6 cm. distance on each side of the neck; the dose and distance in each instance depending on the needs of the individual case. If sufficient radium is not available to do this properly, then efficient *x*-radiation should be used as the second choice.

The decision as to the method of internal application is not so simple. In our earlier work we made extensive use of radium emanation tubes filtered by 1 mm. and 2 mm. of platinum placed end to end in small rubber tubing and introduced within the lumen of the cocainized larynx. The dosage ranged from 100 to 300 mc. hrs. per tube. This provides a very efficient dosage of gamma radiation all about the tubes and serves a useful purpose in intrinsic lesions involving practically the whole of the interior of the larynx. It has many disadvantages. It is difficult even with very strong tubes and in a well-cocainized throat to retain the radium accurately in place long enough to give proper dosage unless a tracheotomy has been done. For all extrinsic growths it is purely a gunshot procedure and very inefficient. It furnishes radiation to normal and diseased tissues alike, depending on their proximity to the center of radiation, and from this, unwarranted damage may result. The method of treatment by intubation, and radium application within this, as advocated by most of the Spanish workers, is essentially the same thing from a physical standpoint and is open to the same criticism.

The greatest advance in our internal treatment has been through the introduction of radium emanation tubes directly into the growth. These are fine capillary glass tubes approximately 0.3 × 3 mm. in size, containing radium emanation. This emanation decreases in value at the rate of approximately 15 per cent per day. It is evident therefore, that the exact dosage to be delivered by these tubes can be calculated at the time of introduction. One mc. of radium emanation buried interstitially and left *in situ* until exhausted gives a dosage of 132 mc. hrs. The emanation in this form is entirely unfiltered except for the thin wall of the glass tube, which removes little more than the alpha rays. Hence the full effect of both beta and gamma rays is obtained, and since the radiation is extended over several days, a larger dose can be given. The tubes are small and readily introduced through fine trocal needles, so that accurate distribution can be made throughout the growth, especially toward the deep infiltrating base where most efficient radiation is required. We use curved trocar needles for application by the indirect method and straight needles for the direct method. In the majority of cases I prefer using the direct method under local anesthesia.

There is some danger, of course, from introducing mixed infection deeper in the tissues, but this is very slight, especially if care is taken to avoid introduction through the ulcerating surface wherever possible. We have never had trouble from the glass emanation tubes as foreign bodies. They are either expelled and expectorated with minute particles of slough later on or are encysted in scar tissue as a result of the inflammatory process created by the radium. In our earlier work with buried emanation we made the mistake of using tubes of too strong individual values. As a result, very severe reactions with considerable sloughing were encountered. We now feel that such reactions are both unnecessary and unjustifiable. Tubes of approximately 1 mc. each permit of most adequate dosage with uniform distribution and a minimum amount of destruction of tissue. This method is applicable in the majority of intrinsic lesions and in in all extrinsic lesions. We have found it practical to bury amounts of 1 to 6 or 7 mc. in intrinsic growths and as high as 15 mc. in some bulky extrinsic growths. The size, shape and location of the individual lesion, together with the local anatomical relations, must be the guide to dosage in each instance. Apart from the problem of beta radiation obtained, these emanation tubes for laryngeal work have a very definite advantage over needles containing radium salt in that they are smaller, cause less trauma, and cannot be dislodged as a needle with a string at the end might. In addition, the whole procedure is over at one sitting and there is nothing left to be removed later.

For a certain limited group of localized, relatively superficial, intrinsic growths, we employ another method of unfiltered radium application to the surface. This consists of a small glass bulb 6 to 8 mm. in diameter, containing 500 or 600 mc. of emanation and mounted in a protecting metal cone with paraffin. The cone is open at its base and to the apex a long flexible wire is attached. This permits of holding accurately in place by the indirect method a very large quantity of unfiltered radium emanation for a time long enough to give an intensive dose. A few minutes is sufficient and, in addition to accurate localization, the surrounding normal tissues are protected from injury.

In the application of any or all of these methods to a favorable case, maximum doses should always be given. Best results are obtained by aiming at complete regression from a single dose. The inflammatory reaction excited by a first application makes difficult the differentiation of malignant from inflammatory tissue. The inflammatory reaction results in the formation of new connective tissue which in turn protects remaining malignant cells. Furthermore, the repeated induction of these uncomfortable reactions within the larynx is devitalizing to the patient. This refers more especially to the use of buried emanation tubes. There is no objection to the repetition of heavily filtered doses externally as long as the skin remains in good condition and edema internally is not marked.

PALLIATIVE TREATMENT BY RADIUM

In considering radium as a palliative agent, we must reverse the plan outlined for its radical use. Where no reasonable hope for complete regression of disease can be entertained, the patient's comfort must be given first place and radium dosage kept down to such a point that no severe reactions will be encountered

In all these cases, heavily filtered radium applied externally at crossfire is indicated. A considerable amount of retardation of growth is produced through the direct effect of radiation on tumor cells, while the fibrosis excited tends to limit the growth locally and prevent distant extension. In certain cases emanation, in small doses, may be buried in the primary growth to advantage, but large doses applied in this manner are definitely contraindicated. I am confident that, in our earlier work especially, we have been guilty of many grave errors in this direction.

In many advanced cases cervical nodes are present on one or both sides. Emanation buried in these has a two-fold value. It is not only the most efficient method of affording palliative relief to the nodes, but they in turn serve to hold a considerable

quantity of emanation which by reason of its gamma radiation exerts a marked inhibitory effect on the primary growth. Thus the interior may be satisfactorily held in check for a considerable period without subjecting it to the inflammatory reaction of a dose applied directly. We feel that this has been a distinct advance in our palliative technique.

Time does not permit of a detailed discussion of treatment of extension of the disease to cervical nodes. In general, our plan is that outlined in a report last year of the treatment of cervical nodes secondary to intraoral carcinoma. No surgery is done in the neck unless a definite node is palpable. If the primary growth warrants it, a unilateral neck dissection is done under local anesthesia and radium emanation tubes buried in the wound at the points of severance of the lymphatic channels. Advantage is taken of this surgical exposure to ligate the external carotid artery and also to bury emanation as near the base of the primary laryngeal growth as possible. If the primary growth is unfavorable or the nodes infiltrating beyond their capsules, no dissection is attempted. Instead, emanation tubes are buried uniformly through the skin, depending on the merits and anatomical conditions of the individual case.

THE COMBINATION OF SURGERY AND RADIUM

Our experience does not warrant expressing an opinion on the value of radiation followed by radical removal. In the small series in which we have attempted this plan, the disease was so far advanced that the surgical procedure was with one exception shown to be ill-advised. Based on our information in general, however, it would seem that pre-operative radiation would be very valuable to those following the radical surgical methods. Postoperative radiation of squamous cell carcinoma is too much of a gun-shot procedure to be considered of much value.

In addition to the combination of surgery and radium already referred to, in the neck, we have employed surgical exposure to advantage during the past year in another direction. Certain deeply infiltrating growths are very difficult to localize by the intralaryngeal methods, and here we have employed laryngofissure as a means of more accurately exposing the growth and inserting emanation tubes.

STATISTICS OF TREATED CASES

The foregoing suggestions for treatment of malignant disease of the larynx are based on a series of 156 cases treated at the Memorial Hospital during the past five years.

Of these, 20 cases were classed as primary operable intrinsic carcinomas. Seven of this group are now free from clinical evidence of disease: one for three and one-half years, 3 for two and one-half years, one for two years, one for one year, one for eight months.

One of the cases now well two and one-half years had an involved cervical node and was treated by surgical dissection of the neck plus radium emanation buried in the wound. The case reported well for eight months and had a severe secondary radium reaction recently, but this is now subsiding satisfactorily.

Four of these cases, only, were verified by microscopic section, and for this we must expect to be severely criticized—perhaps justly so. However, we have here, as elsewhere in the body, followed out our principle of refusing to take a section if it seemed to be not in the best interest of the patient. The dangers of opening up avenues of extension deeper into normal tissues, of infection, and of edema must be reckoned with where the growth is not bulky and fungating. Under such circumstances we have favored the clinical opinion of observers trained in the diagnosis of malignant disease even at the risk of criticism from some quarters.

Seven cases are progressing favorably with reasonable hope for a complete regression of disease, although it is too early to draw any definite conclusions.

One case treated over two and one-half years ago had a violent reaction from the use of tubes of too high individual values, infection and sloughing resulted and a laryngectomy was done in another institution. This patient is reported free from disease at present, but cannot be classified as benefited by radium.

Another case treated one year ago had a complete disappearance of disease after four months, but since then has been lost to our observation.

Four cases were complete failures. One of these returned to his home at some distance from New York, treatment was neglected, and he has been recently reported dead. Another died of pneumonia following tracheotomy. A third was unimproved, laryngectomy was resorted to, and death from infection resulted four weeks later. The fourth case is still living, but is steadily going downhill.

Of the entire series, 51 cases were classed as intrinsic inoperable. Forty of these were primary and 11 recurrent. Of the primary cases, 8 had definitely involved cervical nodes, and of the recurrent cases, 3 had cervical nodes involved, one of them recurring locally later: 2 were recurrent in the nodes only, following total laryngectomy. The 32 primary cases without involvement of nodes were inoperable because of extensive local lesion coupled either with poor general physical condition or advanced age or both.

In this group of 32 cases, 2 were malignant granulomas. Both of the malignant granulomas have been free from clinical evidence of the disease for periods of a little over a year. One case of carcinoma remained free from disease for one and one-half years, after which time it was lost track of. Another case, treated ten months ago, is reported by his laryngologist in Cuba, free from disease. Nine cases are showing continued palliative improvement over periods of two and one-half years to six months. Seven cases showed temporary palliation over periods of two years to six months, and then either died or are at present going downhill. Ten cases were unimproved and quite possibly made worse. Two cases were lost track of. Of the 8 primary intrinsic inoperable cases with cervical nodes, one case has received palliative relief for eight months to date, but the other 7 have been totally unimproved. Of the 11 recurrent cases, one has shown a very striking result: after heavy radiation a total laryngectomy was done and she has now remained well for five years. Three cases are too recent to draw any conclusions. Three have received palliative relief for six to eighteen months. Three were totally unimproved, and one lost track of.

All of the extrinsic growths in our series have been classified as surgically inoperable. Twenty-nine were primary and one recurrent without cervical nodes; 53 were primary and 2 recurrent with cervical nodes. All were classed as carcinomas, with one exception—a lymphosarcoma—although all were not confirmed by microscopic section.

Of the 31 cases without cervical nodes, four, all confirmed by sections, are free from clinical evidence of disease at present. One for two years, two for one and one-half years and one for fifteen months. Three show palliative improvement to date over periods of four to twenty months. Four were improved for eight to twelve months and then began going down. Three are too recent to classify. Eleven were unimproved, and would have been better off had no treatment been given; and five were lost track of.

Of the 55 extrinsic cases with cervical nodes, two are now free from clinical evidence of disease for periods of ten and twelve months following the use of buried emanation in the primary growth and a combination of surgical dissection and buried emanation in the neck. Twelve cases show palliative improvement to date over periods of four to twenty-two months. Two cases, while showing a satisfactory initial response, are too early to classify. Ten cases were temporarily benefited over periods of six to twelve months. Twenty-one cases were totally unimproved and eight we have been unable to trace.

SUMMARY

1. While radium offers hope to a larger number of cancers of the larynx than the older methods, its use must be considered, to a certain extent, experimental as yet.

2. Before treatment of a laryngeal neoplasm is undertaken, proper classification, based on what can be reasonably hoped for, should be made, and the method and intensity of treatment governed accordingly.

3. While treatment of primary operable intrinsic cancer of the larynx is permissible,

the evidence to date does not warrant advocating it as the agent of choice.

4. It is suggested that the pre-operative use of radium in operable cases would add materially to the end result.

5. Surgical exposure may frequently be used to advantage in radium localization.

6. The radical use of intensive radiation is permissible in cases offering a reasonable hope for complete recovery.

7. The conservative use of radiation in inoperable cases offers palliative relief in a large percentage.

8. Radium should be withheld in the very advanced cases.

BIBLIOGRAPHY

Ewing, J. Neoplastic Diseases, 1st Edition. Philadelphia, 1919.

Janeway, H. H. Radium Therapy in Cancer at the Memorial Hospital (First Report 1915–16). New York, 1917.

Moore, Irwin. Intrinsic Cancer of the Larynx. London, 1921.

MacKenty, J. E. The technique and after-treatment of hemi-laryngectomy and total laryngectomy. *J. Am. M. Assn.*, Sept. 15, 1917, lxix, 863–868.

Jackson, Chevalier. Peroral Endoscopy and Laryngeal Surgery. St. Louis, 1915.

Semon, Sir Felix. Some points in the diagnosis and treatment of laryngeal cancer. *Brit. M. J.*, Feb. 2, 1907, i, 241–248.

Gluck, Sorensen. Die Resektion und Exstirpation des Larynx, Pharynx, und Osophagus. *Handb. d. spez. Cbir. d. Obres*, 1913, iv, 100–105.

Butlin, H. T. On the Results of Operations for Cancer of the Larynx, with an Analysis of 307 Cases. London, 1908, p. 8.

Freer, O. T. Radium emanation in the upper air passages as compared to radium: A method of applying it with especial reference to laryngeal carcinoma. *Illinois M. J.*, Aug., 1921, xl, 85–90.

Amersbach, K. Zur Strahlen-behandlung des Kehlkopfund Rachenkarzinoms. *Deutscbe Med. Wcbnscbr.*, Nov. 11, 1920, xlvi, 1269–1271.

Coakley, C. G. Epithelioma of the larynx treated by radium: *Laryngoscope*, 1916, xxvi, 1250–1253.

Alexander, G. Beitrag Zur Radium und Röntgenbehandlung der Kehlkopfkarzinoms: *Wien. klin. Wcbnscbr.*, Jan. 1, 1920, xxxiii, 12–14.

Guisez, J. Traitment du Cancer de l'oesophage et du larynx par les Applications de Radium: *Paris méd.*, May 8, 1920, x, 392–397.

Candela, A. Procedimientos de Eleceion par la Laringectomia Total. Revista Espanola de Laring. *Oto-rbino-laryngol. internat.*, 1919, x, 60.

Hernandez S. Ligeras Consideraciones Sobreel, Tratamiento del Cancer Laringeo: Revista Espanola de Laring. *Oto-rbino-laryngol. internat.*, 1919, x, 106.

Falgar. Laringuectomia y Radium en el Cancer Laringeo: Revista Espanola de Laring. *Oto-rbino-laryngol. internat.*, 1919, x, 245–252.

Casadesus. Tirotomia Combinada con Radiumterapie por Epithelioma Laringeo: Revista Espanola de Laringo. *Oto-rbino-laryngol. internat.*, 1920, xi, 253.

Botey, Ricardo. Tratamiento del Cancer Laringeo por la Intubation Radifera: Revista Espanola Laring. *Oto-rbino-laryngol. internat.*, 1918, ix, 233.

Mi Experiencia Sobre el Metado de Gluck en la Larienguectomia: Revista Espanola Laring. *Oto-rbino-laryngol. internat.*, 1919, x, 102.

Tratamiento del Cancer Lariengea por la Intubation Radifera: *Rev. de med. y cirug. pract.*, 1918, cxviii, 289.

Lannois. La Radiumtherapie des Tumeurs en oto-rhino-laryngologie. *Bull. Acad. de méd.*, 1919, lxxxi, 638–645.

Jones, B. Seymour. An apparent cure of endothelioma or sarcoma of the trachea with radium emanation: *J. Laryngol.*, 1918, xxxiii, 242–244.

Delavan, D. B. Statistics of the operations for the relief of malignant disease of the larynx: *N. York M. J.*, 1900, lxxii, 449.

Quick, Douglas. The conservative treatment of cervical lymphatics in intra-oral carcinoma. *J. Am. M. Assn.*, Aug. 6, 1921, lxxvii, 436–441.

DISCUSSION

Dr. Pfahler. I wish to refer for just a minute to some work which I presented last Saturday before the Radiological Society, which I think is rather new. That is the implantation of radium needles through the hyothyroid membrane, for carcinoma of the larynx. First of all, I request that a tracheotomy be performed; the first of the treatment being given by external radiation, and about a week after this radium needles are inserted through the hyothyroid membrane, approximately on each side if both are involved, or five on one side if only one side is involved. If the larynx is detached from the side you can pass the needles down through the hyoid inside. You are passing through healthy tissue, you have the needles retained exactly where you put them, and you remove them at the end of the period, which in my work has been eight hours. I have had only eight cases but the results have been more encouraging than anything I have seen in these cases.

Dr. Clark. The successful treatment of malignant disease of the larynx requires most careful consideration. If seen early, laryngectomy offers a fair chance of success, as shown by Crile, Lewis and others. But, since the advent of radium, *x*-rays, desiccation, and coagulation methods, laryngectomy need be practiced only in advanced cases, and then always in conjunction with radium or other methods. I have given up the application of radium to the larynx through an endoscope. Much better results have been obtained by the following technique: A preliminary tracheotomy is invariably performed, after the lapse of about ten days a laryngotomy, or longitudinal-slit operation is performed and both sides of the larynx retracted. The lesion may then be palpated and inspected at close range.

If the growth is localized and does not extend through the cartilage, it is thoroughly desiccated and then curetted away, which latter operation can be accomplished without hemorrhage. Radium needles of proper size are then inserted wherever there appears to be any chance of remaining disease. Excellent results have been obtained in several cases by employing this technique. The operation described appears not to be hazardous and healing is very rapid. The tracheotomy tube may later be discarded, and, unless the cords have been destroyed, the voice will be little impaired. If the lesion is so extensive as to involve the cartilage all the way through, laryngectomy is performed, followed by desiccation, or radium needles, or both. The *x*-rays, or radium, should be applied at subsequent intervals from the outside.

The foregoing mode of procedure has in my hands been much more satisfactory than others previously tried.

BOOK REVIEWS

PROTEIN THERAPY AND NONSPECIFIC RESISTANCE, by William F. Petersen, M.D., Associate in Pathology, University of Illinois, College of Medicine, Chicago, Illinois; with an Introduction by Joseph L. Miller, M.D., Professor of Medicine, Rush Medical College, University of Chicago, Chicago, Illinois. Cloth. Price $4.50. Pp. 314. New York: The MacMillan Company, 1922.

At first glance this book would not seem to be of particular interest to the radiologist; but an investigation of its contents reveals the fact that much food for thought is offered for the radiotherapist who wishes to understand the whys and wherefores of the effects produced by the therapeutic measures in his specialty.

Nonspecific therapy is recognized even by immunologists as one of the factors of resistance to disease. How far-reaching the field of nonspecific stimulation is in its various modifications becomes apparent from a consideration of the number and the character of the agents which have been employed to bring about therapeutic results. Even the purely physical and mechanical means—including irradiation, electricity, baths, massage, etc.—must be included in the survey.

To all those interested in the treatment of infections—and this includes both physicians and immunologists—this book will be most welcome, presenting as it does in a comprehensive manner a complete analytical review of the subject, which will be of assistance in furnishing a basis for further carefully controlled studies.

JAMES T. CASE.

THE PATHOLOGICAL GALL-BLADDER, by A. W. George, M.D. and R. D. Leonard, M.D. Contains 143 pages besides 135 Roentgen-ray studies on 44 full page plates, of which three are photographs and two text illustrations. Price $10. Paul B. Hoeber, New York, 1922.

This monograph presents the ideas of those who have done most to advance and popularize *x*-ray examinations of the gall-bladder region in America.

The technique which the authors have found most satisfactory is carefully described.

The chapter on interpretation is the most important one in the book. Lesions of the gall-bladder are considered from two angles. The visualization of gall-stones and the gall-bladder is regarded as direct evidence, while the effect produced by the pathological gall-bladder upon the surrounding structures is regarded as indirect evidence.

The illustrations, 135 in number, are well done, and the captions for the illustrations are in English, French and Spanish. The volume is a beautiful example of the book-maker's art. This book will be much appreciated by all who are interested in lesions of the right upper abdominal quadrant.

THE AMERICAN JOURNAL OF ROENTGENOLOGY
Editor: H. M. IMBODEN, M.D.
Associate Editors: JAMES T. CASE, M.D. H. K. PANCOAST, M.D. J. S. SHEARER, PH.D.
Publisher: PAUL B. HOEBER, NEW YORK

Issued Monthly. Subscription, $6.00 per year. Advertising rates submitted on application. Editorial office, 480 Park Avenue, New York. Office of publication, 67-69 East 59th Street, New York.

Information of interest to all readers and lists of officers of The American Roentgen Ray Society and The American Radium Society will be found on the two pages preceding Table of Contents.

TWENTY-THIRD ANNUAL MEETING THE AMERICAN ROENTGEN RAY SOCIETY
LOS ANGELES, CAL., SEPTEMBER 12, 13, 14, 15, 16, 1922
Headquarters, Meetings and Exhibits: Hotel Ambassador, Los Angeles, Cal.

EXTRACT FROM A PAPER ON MEASUREMENTS USED IN RADIOACTIVITY AND THE RADIUM STANDARD

BY MADAME P. CURIE

PARIS, FRANCE

THE International Radium Standard was prepared during the month of August, 1911. The salt used was taken from the very pure radium chloride reserve, weighing about 0.4 gm., that I had prepared in 1907 for the purpose of obtaining the atomic weight of radium. The great purity of this salt had been ascertained by spectrum analysis; its atomic weight is 226.5. The salt had been stored with precautions so as to eliminate all risks of accident; one part of it had been used for the preparation of metallic radium and of standard solutions.

The manipulations made in order to bring the salt back to a definite state were the following: A quantity of water containing a small amount of hydrochloric acid was added to the salt; the salt dissolved nearly completely in it, leaving a very small quantity of an insoluble salt, as is always the case after a time, probably due to the corrosion of the vessels, even when all the moisture has been eliminated. This residue was removed by filtration and a very small quantity of lead acetate was added to the clear solution; it was afterwards treated with hydrogen sulphide. The lead sulphide, while being precipitated, was expected to draw with it the total amount of radioactive lead (radium D), of radium E, and of polonium, (radium F) formed in the radium salt in the course of four years. After the sulphides had been removed by filtration, the solution was evaporated until dry. The salt was dissolved again in a mixture of water and pure hydrochloric acid and the solution was concentrated so as to crystallize. When cool, the crystallization water was decanted and the crystals were washed in pure concentrated hydrochloric acid, then dissolved again in a mixture of pure water and pure acid so as to obtain crystals again. The crystallization was of a beautiful character, and some large crystals, needle-shaped and very elongated, were formed. The crystallization water was plentiful, because the crystallization took place in a very acid medium, and was decanted. The crystals were first dried in a water-bath and then in an oven at a temperature of 150° C. This temperature was sufficient to bring back the salt to an anhydrous state and to the formula $RaCl_2$.

The tube was then prepared. Its appearance was that of a glass tube with very thin walls; its inside diameter was 0.9 mm.; wall thickness, 0.27 mm.; clear glass. The extremity of the tube was drawn and

closed over a platinum wire, using a flame to accomplish the operation; this wire was very fine and extended inside the tube. The purpose of this wire is to keep any electric charges from accumulating inside the tube by establishing a communication with the outside. A small glass cap fitting over the tube was prepared, and the tube, together with the cap, was carefully weighed. It was feared that the salt would accumulate water during the filling operation, and that it would be difficult to expel the water afterward on account of the shape of the tube. To avoid this, the filling operation took place in a warm atmosphere. The vessel with the crushed crystals and a stirrer were placed on a thick metal plate and heated. The temperature of the air surrounding the crystals was about 80° C. The tube to be filled was kept constantly in that warm air. After being sufficiently filled, the tube was fitted with its cap and alternately weighed, put back in the oven, heated at 150° C., and left to cool down to a normal temperature while in a dry chamber. During these operations the weight of the tube and its contents did not change beyond the limit of $\frac{1}{50}$ of a mgm. The tube was then sealed in a flame at a point very near the top of the salt which occupied the entire length of 32 mm. It was then made sure that no salt had stuck to the removed section, the quantity of which could have been detected using a scale. It has been possible to accomplish the filling in such good conditions and without the salt sticking to the walls with the help of a thorough dessication of the matter. Figure 4 is an illustration of the tube.

The balance used was a Curie balance of the rapid check type and fitted with a microscope; it was adjusted so as to be sensitive to $\frac{1}{100}$ of a mgm. The weights used were accurate and in conformity with the standards. A tube similar to the principal tube was used as tare.

The salt reached a definite state and an invariable weight equal to 0.02199 gm. of $RaCl_2$ (anhydrous chloride) within a limit of about $\frac{1}{50}$ of a mgm. The weight of the tube is 0.1022 gm. The quantity of metallic radium enclosed in the tube weighs 0.01675 gm.

Due to the thinness of the glass and to the elongated shape of the tube, the fraction of gamma radiations absorbed by the salt and the walls of the tube probably does not reach 0.5 per cent.

Nearly the whole length of the tube is occupied by the salt; such a condition is of advantage as regards the accuracy of measurements, for it may be affected by a shifting of the salt as a consequence of jolts. On the other hand, the question might arise whether by reducing thus the free space there are any risks of jeopardizing the safety of the tube due to the fact that the continuous accumulation of gases might cause it to explode. But as the salt has been carefully deprived of all its water of crystallization, the production of explosive gases, a usual occurrence with a hydrated salt, is not to be feared. The only gas production to be considered is that of helium; this cannot be avoided, and its value is about 2.5 c. mm. per year for the quantity of radium enclosed in the tube referred to. As the volume of the tube is about 25 c. mm. and the actual space occupied by the particles of matter cannot be more than 6 c. mm. a period of eight years will elapse before the pressure due to helium production equals the atmospheric pressure, the gas being supposed to be set free. (In reality the gas stays within the salt, but may be driven out by an accidental overheating of the tube.) As the tube was sealed while hot, the initial air pressure decreased when cooling and was then less than atmospheric pressure. It may be said that it will require fifteen years before it may be advisable to open the tube at its pointed extremity so as to allow any excess of helium gas to escape.

At the time the International Standard was being prepared in France, a similar operation was carried out at the Radium Institute of Vienna, where several standard tubes containing different quantities of anhydrous radium chloride were being prepared with a carefully purified salt owned by the Academy of Sciences of Vienna.

It seemed then possible to take the final steps concerning the standards, and to call for that purpose a meeting of the Committee to whom this work had been intrusted by the Brussels Congress.

The meeting of the International Committee was called in Paris at the end of March, 1912. Seven members were present. The work of the Committee was to compare the different standards prepared and to determine rules for their use.

The comparison of these standards was made by measuring the gamma radiations. The measuring apparatus was prepared by the Radioactivity Laboratory of the Faculté des Sciences of Paris under the direction of M. Debierne. However, its installation was not made in that laboratory, due to the fact that the air in these rooms had a spontaneous conductivity much higher than air in a normal state, and this condition is unfavorable for accurate measurements. Due to the kindness of Prof. Lippmann, the apparatus was set up in an inactive room which was part of his department.

The comparison was made by two different methods: First, by a compensation method in use by the Paris laboratory; its characteristic feature is the use of a large plate condenser, especially constructed for this event. The dimensions of this apparatus are the following:

Diameter of plate E	50 cm.
Diameter of cylindrical box P	52 cm.
Distances from plate E to bases of the box	3.5 and 2 cm.

A lead shield one cm. thick was laid on top of the box P. The tube to be tested was placed on a piece of paper laid on the shield. The current produced in the chamber was measured by a device made up of an electrometer and a piezoelectric quartz. The effects observed when shifting the tube to another position were carefully noted as regards the value of the current. These effects were not perceptible for slight differences in position from the center.

The second method is of the same kind, but slightly different. The apparatus was set up under the supervision of Mr. Rutherford. A steady current produced in an auxiliary ionization chamber containing a quantity of uranium is compensated by the current produced in the principal ionization chamber by the action of the tube placed at the proper distance. As the distance from the tube depends on its radium content, it is necessary that the law governing it should be known, in order to compare different quantities of radium to one another. With this method, the conditions are not quite as nearly the same as with the first method for the comparison of tubes.

With both methods, results were obtained which agreed with each other and which showed for the different standards a very satisfactory similarity. The differences were estimated to be about 0.2 per cent, which is within the allowable limits of experimental error.

It is quite remarkable that these results were obtained with standards prepared in France and in Austria respectively, and that the pure salts used had been prepared independently in these two countries. This shows, on one hand, the confidence that may be placed on the composition of anhydrous radium chloride, and, on the other hand, the high degree of perfection of the methods using gamma radiations for the measurement. By these means, a basis for the measurement of the radium content has been established, and can be relied on with perfect confidence.

Comparisons were made easy by the fact that the glass walls of the tubes were not only thin, but were also of the same thickness for each of the standards.

After the experiments the Committee made the following statements:

1. The Standard prepared by Madame Curie has been given the preference as International Standard and it has been decided that this standard should be kept at the *Bureau International des Poids et Mésures* of Paris, with the consent of the director of this Institution. The International Standard shall be used solely for the measurement of secondary standards intended for different countries.

2. One of the standards prepared in Vienna shall be kept at the Vienna Institute as an auxiliary standard ($RaCl_2$-31.17 mgm.).

3. The secondary standards shall be prepared using for each from 10 to 40 mgm. of a radium salt whose purity is at least 90 per cent; they will be similar in

shape to those prepared in Vienna.* They shall be measured, first in Vienna, then in Paris, and a certificate shall be issued stating their radium content.

4. As the radium used for the International Standard was the property of Madame Curie, the Committee recommended that the necessary steps be taken so that an equivalent amount of radium be given to Madame Curie by the countries involved.†

We still have to consider the actual state of the International Standard and discuss the evolution laws as they have been predicted, as well as their influence on the value of the Standard.

From a chemical standpoint, at the time the tube was sealed, the salt of the standard was a pure and anhydrous radium chlorid, in conformity with the formula $RaCl_2$. From a radioactive standpoint, the salt has since its crystallization become the seat of an accumulation of emanation and of its subsequent products. From this standpoint, the nature of the salt reached a stationary state in about one month; the quantities of emanation, of Radium A, B, C, which are now formed inside the tube are in a state of radioactive equilibrium with the salt and are present in small amounts (less than $\frac{1}{10.000}$ of a mgm.).

Nevertheless the part they play in the emission of radiation is considerable; in fact, the gamma radiation can be attributed to radium C. As a result of the slow evolution which took place thereafter, substances D, E and F have accumulated and their relative amounts will increase during a period of about one hundred years. Of these substances, Radium E alone seems to emit gamma radiations; but these radiations are far less penetrating than those emitted by Radium C, and it may be assumed that they are an unimportant factor for measurements based on radiations that have passed through a sufficient thickness of lead (1 cm.). This point therefore should be carefully determined. If it is admitted, for the time being, that no consideration should be given the slow evolution products, it must be expected that the very penetrating gamma radiations will follow the law of radium evolution; that is, will decrease according to an exponential law, with a period of two thousand years. Whence the decrease over a period of one year should be about 0.04 per cent, so that during a period of ten years the standard can be considered as invariable. During a subsequent period of from twenty to thirty years a slight correction, approximately known, would permit of still using it; this is sufficient to obtain the services that are anticipated from it.

One might wonder, now, if radium extracted from uranium ores could not be accompanied by a trace, defying the most sensitive balance, of any other radioactive substance than its derivatives and capable of emitting very penetrating gamma radiations. Of these, the substance most to be feared is mesothorium. This substance is a derivative of thorium, which is generally present in uranium ores. Mesothorium accompanies radium in the chemical separations of the substances in the ore and in the fractional crystallization. This substance is the starting point of a series of derivatives which follow a complex law; resulting finally in the emission of gamma radiation which can be compared to those of Radium C as far as their penetrating power is concerned. The presence of mesothorium in radium therefore would affect the evolution law of the gamma radiation, and hence the accuracy of radium measurements. Fortunately, there are some uranium ores accompanied by only a very small proportion of thorium; for this reason, the ores can contain only a quantity of mesothorium too small to give rise to the difficulties mentioned above. This is the case with the St. Joachimstahl pitchblende, which contains about one k. of thorium per 50,000 k. of ore, consisting of 53 per cent uranium oxid, this amount being capable of yielding 3.7 gm. of radium. (See St. Meyer and Hess, Vienna Academy of Sciences, 1912.) The gamma radiation of one k. of thorium is absolutely negligible compared to that of 3.7 gm. of radium (about 3 hundred-

* The diameter of the Vienna tubes is 3.2 mm., and the salt occupies only one part of the tubes. The shape of the International Standard is more nearly perfect, but is more difficult to obtain.

† This question was settled as soon as the text of the statements was published. Dr. and Mrs. G. P. Beilby made an offer to the Committee to assume the expenses of replacing the International Standard, wishing to give their offer a character of special friendship toward me, for which I thank them most sincerely.

thousandths) and the presence of mesothorium can in that case be of no noticeable inconvenience. This applies to the International Standard as well as the Vienna standards which were prepared with radium extracted from St. Joachimstahl pitchblende.

The International Standard can therefore be used with great safety. This degree of safety can be further increased by preparing under similar conditions a tube, the activity of which can be compared from time to time by means of an absolute measurement apparatus (method of the piezoelectric quartz, for instance). This will permit the experimental determination of the law of the evolution of the standard in the course of time.

In conclusion, the adoption of an accurately known standard will result in the following services:

1. From the standpoint of the science of radioactivity: It insures an agreement among the numerical results obtained in various laboratories by the use of a given amount of radium. In case results should not agree, the experiments would be repeated and possibly lead to the discovery of new facts.

2. From the standpoint of medical applications: It insures a judicious use of the physiological properties of the radiations due to the fact that it will be possible to measure exactly and with perfect safety the intensity of the radiation source used.

3. From a commercial standpoint: It establishes a basis for the radium industry and renders it secure, due to the fact that it will be possible to know exactly the amount of radium contained in the quantities sold; this will promote complete confidence between the manufacturers and the buyers. This service can be extended to the sale of mesothorium, as I have explained before.

Taken as a whole, the points explained in this article show plainly the high general value of the International Radium Standard. It may be rightfully anticipated that the initiative taken in this connection by the Radioactivity Congress of 1910 will be fertile in happy consequences, showing that real progress is being made towards various achievements.

FOURTH ITALIAN CONGRESS OF RADIOLOGY, BOLOGNA, MAY 9–11, 1922.

The Fourth Congress of Radiology held its opening meeting on May 9th at the Rizzoli Institute. Professor Busi presided. Professor Corbino delivered a lecture on the physical basis of radiation therapy, emphasizing the progress made in this branch of physics.

In the afternoon Professor Balli read a paper on "The Limits between the Normal and Pathological in the Radiology of the Digestive Tract." He discussed numerous diagnostic problems and illustrated them by lantern slides. Papers on the same subject were also read by Professors Alessandrini, Saraceno, Arnone and Pesci. Papers on the *x*-ray diagnosis of pulmonary and cardio-vascular lesions were read by Professors Ceresole, Gortan, Siciliano, Maragliano and others.

The most important paper of the next session was on "The *X*-Ray Diagnosis of Duodenal Ulcer," by Dr. Tandoia of Naples. Professors Parola, Ponzio, Palmieri, and Vespignani took part in the discussion. An executive meeting of the Italian Radiological Society followed. Professor Corbino was unanimously elected honorary president of the Society and of the Fifth Congress.

At the afternoon session several papers on deep therapy were presented. From these and the extensive discussion which followed, it may be concluded that in many cases deep radiotherapy is the method of choice for the treatment of neoplastic diseases of the uterus and breast. In spite of the progress which has been made in the biological, physical, and therapeutic aspects of the work, we cannot really speak as yet of radiotherapy as a cure for cancer. Papers on deep therapy dealing primarily with technique were read during the morning session on May 11th. The German methods advocated by Seitz and Wintz, Friedrich, and Dessauer were discussed. Professor Ceresole made the suggestion that the radiologists who are connected with large institutions undertake systematic researches, and that the results be presented at the next Congress.

Professor Ross , Dr. Pais, and Dr. Spagnolio read papers on the treatment of malaria by *x*-rays. Extensive statistical data were given.

Doctors Tarchini, Vigano, and Conti read papers on radiotherapy in dermatology. Professor Gortan reported some interesting observations on the therapy of brain tumors; Professor Gavazzeni on Basedow's disease.

Mr. Lubostiez brought out some important points in radiographic technique. Mr. Iten explained the Potter-Bucky diaphram and the Victor stabilizer. He also showed moving pictures illustrating the process of the manufacture of the Coolidge tube.

The numerous exhibits of *x*-ray apparatus, showing the progress which has been made, attracted considerable attention.

The Fifth Congress will be held in Palermo, with Professor Scaduto as president and Professor Arnone as vice-president.

CANADIAN RADIOLOGICAL SOCIETY

The Third Annual Convention of the Canadian Radiological Society was held in Winnipeg in conjunction with the Dominion Medical Association, June 20–23, 1922. The scientific session lasted for three days, and included a series of extremely interesting communications. We had the honor to have present with us, contributing to the program, Doctors Lewis Gregory Cole, Russell D. Carman, B. H. Orndorf, R. H. Stevens, F. S. Bissell, and C. J. Sutherland.

The officers elected for the coming year are: President, Doctor L. J. Carter, Brandon; First Vice-President, Doctor C. W. Prowd, Vancouver; Second Vice-President, Doctor J. C. McMillan, Winnipeg; Third Vice-President, Doctor L. T. Pariseau, Montreal; Secretary-Treasurer, Doctor L. K. Poyntz, Victoria. The Executive Committee is composed of Doctor G. E. Richards, Toronto; Doctor A. E. Walkey, Hamilton; Doctor L. K. Poyntz, Victoria.

The rules and regulations governing the Canadian Register of Technicians established in 1921 were adopted, and Doctor L. K. Poyntz of Victoria was appointed Registrar and Examiner.

THE LEONARD PRIZE

The American Roentgen Ray Society is again offering the Leonard Prize in 1923, details for which appear on advertising page ix of this number of the Journal. The manuscripts submitted for the 1921 prize were of a high order of merit and covered a variety of subjects pertinent to roentgenology. It is to be hoped that the contestants for the next prize will be equally zealous in their efforts.

Subscribers to THE AMERICAN JOURNAL OF ROENTGENOLOGY *visiting New York City, are invited to make the office of* THE JOURNAL (*69 East 59th Street, New York*) *their headquarters. Mail, packages or baggage may be addressed in our care. Hotel reservations will gladly be made for those advising us in advance; in this case, kindly notify us in detail as to requirements and prices. List of operations in New York hospitals on file in our office daily.*